



# Population Reports

## Oral Contraceptives — An Update

**Four decades after introduction of the pill, more women than ever are using it. Today's low-dose oral contraceptives are safer and just as effective as earlier pills. Taken regularly, the pill prevents pregnancy almost without fail. Pill users benefit in other ways, too, such as less anemia and protection from certain cancers. Lower doses have reduced the circulatory disease risks of the pill.**

Currently more than 100 million women rely on the pill. It is the top modern family planning method among married women in half of countries surveyed. The pill is most popular in Western Europe, where half of married women use it. It is least used in China, India, and Japan.

A great many women use the pill at some point in their lives. Outside India and China, half of married women who have ever used family planning have relied on the pill at some time. In the US 80% of all women born since 1945 have used the pill. A method so widely used deserves continuing attention from health care programs, providers, and researchers.

### Substantial Benefits and Safer Doses

Research continues to assess the benefits and risks of pill use. The greatest benefit, of course, is effective contraception, which gives women more control over their lives and avoids the risks of pregnancy and childbearing. Among women who miss no pills, only 1 in every 1,000 becomes pregnant in the first year of using even the lowest-dose pills. Because few women use the pill so consistently, however, typical first-year pregnancy rates are about 6 to 8 per 100 women. During breastfeeding, progestin-only pills are highly effective.



Egypt Ministry of Health

### Highlights

Progestin-only is best pill during breastfeeding .....	5
Many women have used the pill ...	6
Method mix changes as contraceptive use grows.....	8
Some cancers prevented .....	11
Lower doses reduce circulatory disease risk .....	13
Perspectives clearer on persistent health issues .....	26

### Contents

Editors' Summary .....	1
Background .....	3
Oral Contraceptive Use .....	4
Benefits of Oral Contraceptives...	10
Health Risks of	
Oral Contraceptives .....	13
Emergency Contraceptive Pills....	17
A Practical Guide to ECP .....	19
Unresolved Health Issues.....	26
Bibliography .....	33

Published by the Population Information Program, Center for Communication Programs, The Johns Hopkins University School of Public Health, 111 Market Place, Suite 310, Baltimore, Maryland 21202, USA.

Volume XXVIII, Number 1  
Spring 2000



tive, complementing the natural protection that breastfeeding offers. They do not decrease milk production.

Oral contraceptives (OCs) offer a variety of other health benefits. For example, by reducing menstrual bleeding, OCs help prevent iron deficiency anemia, which is common and often serious in developing countries. OC use halves the risk of cancers of the uterine lining and of the ovary. Some protection persists for many years after OC use stops. Because estrogen-progestin OCs stop ovulation (release of an egg), they prevent pregnancy outside the womb, which can be life-threatening. Some evidence suggests that OCs reduce risk of colorectal cancer, too.

Compared with earlier, higher-dose pills, current low-dose formulations have considerably lowered the risk of heart attack, stroke, and blood clots in the deep leg veins attributed to OC use. Research has better defined which women would face appreciable risk of heart attack or stroke if they used OCs—women over age 35 who smoke or who have high blood pressure. For all other women, using OCs is clearly safer than childbearing in both developing and developed countries.

## Resolving Uncertainties

Even some of the most persistent uncertainties concerning OCs are now coming into perspective. Research suggests that OCs may somewhat speed up the diagnosis of already existing breast cancers—perhaps because tumors are more readily detected, tumor growth is accelerated, or both. OC use does not increase lifetime risk of developing breast cancer. Among women who use OCs when young and breast cancer is rare, few additional diagnoses of breast cancer would be due to OCs.

Cervical cancer is even harder to study than breast cancer. It may never be clear whether methodological problems in research or an actual cause-and-effect relationship explain recent observations of a slight increase in risk for long-term OC users. Condoms and careful choice of a sex partner offer the sexually active woman the best protection from human papillomavirus, the primary cause of cervical cancer.

## OCs for Emergencies

Combined and progestin-only OCs containing the hormone levonorgestrel can be used for emergency contraception: If the correct dosage is started within 72 hours after unprotected intercourse, it reduces the chances of pregnancy. This has long been known, but only recently has the word spread. Now OC tablets are being packaged as emergency contraceptive pills, and levonorgestrel-only tablets, which are more effective and cause less nausea and vomiting, are being introduced especially for this purpose. While not as effective as regular use of OCs or most other modern methods, emergency contraceptive pills meet a crucial need—another important benefit of one of the world's most widely used family planning methods.

**This report was prepared by Richard D. Blackburn, M.S., Jacqueline A. Cunkelman, M.P.H., and Vera M. Zlidar.** Bryant Robey, Editor. Stephen M. Goldstein, Managing Editor. Design by Linda D. Sadler. Production by John R. Fiege, Merridy Gottlieb, Peter Hammerer, and Deborah Maenner.

The assistance of the following reviewers is appreciated: Marcia Angle, Sharon Camp, Susheela Engelbrecht, David Grimes, John Guillebaud, Robert A. Hatcher, Anne Hyre, James McCarthy, Emma Ottolenghi, Herbert Peterson, Tsique Pleah, Linda Potter, Malcolm Potts, Karin Ringheim, Roberto Rivera, Michael Rosenberg, Lois Schaefer, James Schlesselman, James D. Shelton, Jacqueline Sherris, Jeffrey Spieler, J. Joseph Speidel, David Thomas, James Trussell, Marcel Vekemans, Martin Vessey, and Elisa Wells.

Suggested citation: Blackburn, R.D., Cunkelman, J.A., and Zlidar, V.M. *Oral Contraceptives—An Update*. Population Reports, Series A, No. 9. Baltimore, Johns Hopkins University School of Public Health, Population Information Program, Spring 2000.

### Population Information Program Center for Communication Programs The Johns Hopkins University School of Public Health

Phyllis Tilson Piotrow, Ph.D., Director, **Center for Communication Programs**; Principal Investigator, **Population Information Program (PIP)**

Ward Rinehart, Project Director, PIP

Anne W. Compton, Deputy Director, PIP, and Chief, POPLINE Digital Services

Hugh M. Rigby, Associate Director, PIP, and Chief, Media/Materials Clearinghouse

Jose G. Rimón II, Deputy Director, **Center for Communication Programs**; Project Director, **Population Communication Services**

**Population Reports** (USPS 063-150) is published four times a year (spring, summer, fall, winter) at 111 Market Place, Suite 310, Baltimore, Maryland 21202, USA, by the Population Information Program of the Johns Hopkins University School of Public Health. Periodicals postage paid at Baltimore, Maryland, and other locations. Postmaster to send address changes to Population Reports, Population Information Program, Johns Hopkins University School of Public Health, 111 Market Place, Suite 310, Baltimore, Maryland 21202, USA.

**Population Reports** is designed to provide an accurate and authoritative overview of developments in the population field.

Published with support from the United States Agency for International Development, Global, G/PHN/POP/CMT, under the terms of Grant No. HRN-A-00-97-00009-00. The opinions expressed herein are those of the authors and do not necessarily reflect the views of the US Agency for International Development or the Johns Hopkins University.





# Background

Over the 40 years since oral contraceptives (OCs) were first marketed, they have symbolized modern contraception and have remained the most widely used hormonal method worldwide. OCs provide millions of women with effective, convenient, and safe protection from pregnancy.

OCs also have been the most studied of any family planning method. The study of OCs continues, with new epidemiologic research reported from around the world.

First introduced in 1960, the pill was the leading contraceptive in the US by 1965 (150). By 1970 an estimated 8 to 10 million US women were using the pill, as were an equal number in other developed countries (355, 434).

In developing countries OCs began to appear in the mid-1960s, but high prices put them beyond the reach of all but a few women (378, 434). In 1967 international donor organizations, led by the US Agency for International Development (USAID) and the Swedish International Development Authority (SIDA), began to make OCs available to developing country governments and international family planning organizations (361, 379). Family planning programs in the developing world then began to supply more women with OCs. By the early 1970s an estimated 20 to 30 million married women in developing countries used OCs (434).

OCs remain popular today. With more than 100 million users, OCs trail only voluntary sterilization and IUDs in worldwide use among married women. Among sexually active unmarried women OCs are the most widely used modern method of family planning.

## The Evolution of Oral Contraception

The idea of oral contraception with hormones dates back to the 1920s (170). Not until the 1940s and 1950s, however, did inexpensive, orally effective synthetic hormones become available (120). In 1960, after more than a decade of research, the US Food and Drug Administration (USFDA) approved the first OC. This pill, G.D. Searle and Company's *Enovid-10*, contained 9.85 milligrams (mg) of the progestational hormone norethynodrel and 150 micrograms ( $\mu$ g) of the estrogenic hormone mestranol—about 10 times the progestin and 4 times the estrogen contained in today's pills.

When the pill was introduced, it satisfied women's need for convenient, safe, and reliable contraception. There were some problems, however.

Some pill users experienced such side effects as headaches, nausea, cramps, irregular menstrual bleeding, breast tenderness, or weight gain. These side effects usually are temporary and are not signs of more serious problems. They can be troubling, however, and have led many women to stop using the pill. Also, research in the 1960s and 1970s suggested that estrogen, in the doses used in early OCs, increased the risk of blood clots, stroke, and heart attack (396, 399, 496). Press reports about these findings created repeated "pill scares" and gave OCs an unwarranted aura of danger (150).

Meanwhile, studies found striking evidence of important noncontraceptive benefits of OC use. Most notably, epidemiological studies in the 1980s demonstrated that OCs provide strong protection against endometrial and epithelial ovarian cancer (see p. 11).

The public remains largely unaware of such benefits. In the US, for example, 65% of women surveyed in 1993 could not name one noncontraceptive benefit of the pill. At the same time, over half of respondents believed that OCs pose serious health risks. Moreover, almost two-thirds thought that pill use was at least as dangerous as childbirth (172, 352), which is not the case for most women (182, 295, 306, 413, 454).

Since their introduction, OCs have offered safe contraception for the great majority of women. Still, to reduce common side effects and to minimize the risk of any serious complications, pharmaceutical companies and health care providers have used three approaches:

- To lower the doses of both estrogen and progestin without compromising effectiveness;
- To develop different new progestins;
- To screen women more specifically and to inform them about side effects that they may experience with OCs.

Today's low-dose combined OCs contain less than 50  $\mu$ g estrogen, down from 150  $\mu$ g in the first OC and 50 to 100  $\mu$ g



Lauren Goodsmith

*A Moroccan health worker hands packets of pills to a client. In Morocco pill use has risen substantially, from 14% of married women in 1980 to 32% in 1995. With more than 100 million users worldwide, oral contraceptives remain one of the most popular family planning methods.*



in the OCs of the late 1960s and 1970s. Estrogen doses of 30 or 35  $\mu\text{g}$  ethinyl estradiol are the most common. Progestin doses also have dropped substantially. For example, doses of norethindrone (norethisterone) have dropped from almost 10 mg to 1.0 or 0.5 mg.

The reduction of estrogen doses followed early research that related the likelihood of thromboembolic disorders to the size of the estrogen dose (214). US clinical trials found that estrogen doses as low as 20  $\mu\text{g}$ , combined with a progestin, usually limit pregnancy rates to less than 1 per 100 women per year (27, 28, 39, 141, 209, 248, 400, 404, 499, 543). Also, side effects such as nausea, vomiting, cramps, breast discomfort, and headache occurred less often with less estrogen. Initial menstrual bleeding irregularities are more frequent, however (16, 119, 262, 369).

The progestin doses in OCs vary widely because progestins differ greatly in potency by weight (121). Currently, doses of progestins in the norethindrone family—norethindrone, norethindrone acetate, ethynodiol diacetate, and lynestrenol—range from 0.4 to 2 mg. Pills containing the more potent progestins levonorgestrel, desogestrel, and gestodene use doses of 0.05 to 0.15 mg. The different progestins have somewhat different physiological effects and interact differently with estrogens, possibly modifying the effects of both hormones (48, 467).

Research suggests that lower doses do lower risks for some conditions. For example, as lower-dose pills have come into wider use, findings from epidemiologic studies suggest that risks of OC-related venous thrombosis, heart attack, and stroke have declined. Significantly increased risk of heart attack and stroke is limited to women over age 35 who smoke or women who have high blood pressure (see p. 13).

### Progestin-Only Pills

Progestin-only OCs are a good option for breastfeeding women who want oral contraception because, unlike combined OCs, they clearly do not reduce milk production (see box, p. 5). The progestin-only pill was developed in the early 1970s in response to the reports on estrogen and thromboembolic disease. Each progestin-only tablet contains 0.3 to 0.6 mg of the norethindrone progestins or else 0.03 to 0.0375 mg levonorgestrel. Unlike combined OCs, progestin-only pills are taken continuously, with no hormone-free intervals between cycles. Progestin-only pills have never become widely used. Outside the context of breastfeeding, they are somewhat less effective than combined OCs. Missing progestin-only pills or taking them at differing times of day may increase the risk of pregnancy more than with combined OCs.

### Multiphasic Combined OCs

In the 1970s and 1980s multiphasic OCs were developed. These pills have become popular in some developed countries but are not widely available in developing countries.

The doses in multiphasic OCs change during each pill cycle to keep hormone doses low (78). Like other low-dose OCs, multiphasics appear to provide highly effective contraception when taken correctly. Some clinical trials have observed that multiphasics produce minimal breakthrough bleeding, spotting, and amenorrhea (14, 125, 154, 349). There is little evidence that risks of serious health problems are less with multiphasics than with other low-dose OCs (437).

### Making OC Use Easier

As usually used, the pill often falls short of its potential as a highly effective and convenient contraceptive method. When used correctly, combined OCs provide almost complete protection from pregnancy. In practice, however, pregnancy rates among pill users are about 6 or 8 per 100 women in the first year of use (see p. 10).

Also, as many as half of all new users stop using the pill within a year, and many use the pill intermittently for a few months at a time. While some may not need continuous contraception, this discontinuation rate suggests that many women are having difficulties taking the pill regularly or are dissatisfied. Just as researchers and providers have concentrated on making pill use safer, providers need to focus their attention on making pill use easier. The next issue of **Population Reports** will discuss this need and how it can be met.



*Progestin-only contraceptive pills are a good option for breastfeeding mothers who want oral contraception. This South African brochure explains how progestin-only pills work, their side effects, and advantages and disadvantages.*

## Oral Contraceptive Use Worldwide

Oral contraceptives deserve close and continuing attention. Even though newer contraceptives have become available, in most countries, OCs remain among the most popular methods, and in many countries OCs are the most widely used method of all.

In surveyed countries nearly one married woman in every four who has ever used contraception has relied on the pill at some point in her life. Currently, more than 100 million women use OCs. Data both on ever use and on current use of contraception demonstrate the continuing popularity of OCs.



# Progestin-Only OCs for Breastfeeding Women

For breastfeeding women who have resumed menstruation, progestin-only pills, or "minipills," are a good option if they want to use a hormonal method.\* In contrast to combined pills, there is no risk that progestin-only pills will reduce milk production.

## Why Progestin-Only Pills?

Postpartum women often want to delay another pregnancy, and, indeed, birth intervals of at least two years are healthiest for both siblings (31). Intrauterine and barrier methods offer good postpartum contraception with no effect on lactation. Many women, however, prefer to use OCs. Because combined pills may inhibit milk production, some providers are reluctant to give them to breastfeeding women. If providers will not give OCs to breastfeeding women, however, some women may stop breastfeeding in order to obtain them (21).

Progestin-only pills are a good alternative. They have no adverse effects on lactation. Most research has found either that they have positive effects—increasing milk quantity or improving its nutritional quality—or that they have no effect (72, 145, 211, 296, 530, 531). Women who choose progestin-only pills can use them and continue to breastfeed until lactation naturally stops.

The main comparative disadvantage of progestin-only pills—higher pregnancy rates than combined pills—is offset by the protection against pregnancy that breastfeeding itself provides; during breastfeeding ovulation is uncommon before menstruation resumes and may be irregular even after menstruation has resumed (70). Also, the bleeding irregularities associated with progestin-only pills may not bother postpartum women because they may be amenorrheic or expect irregular bleeding postpartum (297). Progestin-only OCs may not be the best method, however, for women with a history of gestational diabetes (temporary diabetes that develops only during pregnancy). A recent study of women with a history of gestational diabetes found that those who used progestin-only OCs during breastfeeding were almost three times more likely to develop chronic non-insulin-dependent diabetes than women who used nonhormonal methods. Use of combined OCs did not increase the risk of diabetes for women with a history of gestational diabetes (246).

Although combined OCs do affect breast milk, these effects do not seem to harm infants. With combined OCs milk volume usually decreases slightly, even with low estrogen doses (21, 116, 211, 297, 452). Breast milk composition may change, too, although findings vary. Most studies report decreases in mineral content (211, 296). A number of studies have found, however, that reduced milk volume in OC users did not affect their infants' weight gain (57, 208, 452, 529). Studies in Chile reported slower infant weight gain but no other adverse effects on infant health (98, 116, 351). The longest follow-up study found no effects on the health or the physical, intellectual, or psychological development

through age eight of Swedish children whose mothers used combined OCs while nursing (329).

Progestin-only pills do not adversely affect a mother's milk supply, and women using progestin-only pills breastfeed as long as women using no contraception or a method other than OCs (111, 297, 520, 551). In one study 83% of progestin-only pill users breastfed for four months or longer compared with 40% of combined OC users (90).

## When to Begin?

When can breastfeeding women begin to use progestin-only pills? As a general rule, as soon as six weeks after childbirth, according to the World Health Organization medical eligibility criteria for contraceptive methods (538). If a woman is partially breastfeeding and her child receives much other food or drink, six weeks after childbirth is the best time to start progestin-only pills. If she waits longer, fertility may return (190, 255). In contrast, if a woman plans to breastfeed exclusively or fully for a lengthy period, some providers may advise her to wait and offer her progestin-only pills later. Of course, a program can provide any woman with pills immediately postpartum with instructions about when to start them, if contacting her later might be difficult. In all cases it is important that the woman has access to the pills *before* she needs them.

Most family planning programs prefer not to offer any hormonal contraception in the early postpartum months. This is because trace amounts of contraceptive hormones—usually less than one-tenth of 1% of maternal doses—can reach infants in breast milk. No health risks have been linked to such exposure, however (500, 530, 531).

In any case, as noted, fully or nearly fully breastfeeding women who are amenorrheic do not need OCs in the early postpartum period. Fully breastfeeding is more than 98% effective in protecting against pregnancy as long as a mother is: (1) in the first six months postpartum *and* (2) still amenorrheic (237). This rate—two pregnancies per 100 women in the first six months after childbirth—is about the same as typical OC effectiveness (see p. 10).

Program practices about when to offer progestin-only pills to fully or nearly fully breastfeeding women can be based largely on the breastfeeding patterns of the client population. To protect herself from pregnancy, the client should begin progestin-only OCs when menstruation returns or at six months postpartum, *whichever comes first* (84, 237, 485).

*\*Postpartum women have little need of contraception for up to six months after giving birth if they have not resumed menstruating and they are fully or nearly fully breastfeeding—that is, breastfeeding often, day and night, with breastfeeds accounting for at least 85% of the baby's feedings (255, 552). Recent studies have reported a high degree of pregnancy protection for at least six months postpartum and somewhat less protection up to 12 months, if menstruation has not resumed (555).*



## Ever Use of OCs

In 44 of 68 developing countries with survey data on ever use of contraception, more married women have used the pill than any other modern family planning method. In these 68 countries about 40% of married women who have ever used family planning have used the pill at some point. This estimate does not include China, where recent data on ever use are not available. In China and India pill use historically has been limited. If India also were excluded from the estimate, the percentage of married family planning users who have ever used the pill would rise to about 50%.

In some countries pill use has been very common. In Brazil nearly 80% of married women have used the pill at some point, as have two-thirds of married women in Costa Rica, Morocco, and Zimbabwe. Between 50% and 60% of all married women have used the pill in diverse countries including Bangladesh, Botswana, Cape Verde, Colombia, the Dominican Republic, Jamaica, Nicaragua, South Africa, Thailand, and Trinidad and Tobago. Among developing regions, the pill has been most widely used in Latin America, where 55% of all married women have used the pill at some time. More than one-third of married women in the Near East and North Africa have used the pill, while not quite 15% have used it in sub-Saharan Africa (see Table 1).

Similarly, many sexually active unmarried women have used the pill. In 12 of 28 countries with surveys, more of these women have used the pill than any other modern family planning method. Overall, in these countries 52% of women who have ever used family planning have relied on the

pill at some point—39% of all sexually active unmarried women. In Bolivia, Colombia, the Dominican Republic, Guatemala, Nicaragua, and Zimbabwe, between 50% and 60% of sexually active unmarried women have used the pill.

Experience with the pill is probably even more common in developed countries than in developing countries, although data on ever use are not available for many developed countries. In Canada 86% of women surveyed in 1995 had used the pill (38). In the US 80% of all women born since 1945 have used the pill, according to a 1990 estimate (106). Perhaps the highest level of experience with the pill is among German women: For example, 94% of eastern German women ages 30 to 44 have taken the pill (261).

## Current Use of OCs

Worldwide, an estimated 8% of all married women currently use the pill. OCs rank third among all family planning methods currently used by married women. Close to 19% rely on female sterilization, and 13% rely on the IUD. These percentages are greatly influenced by the world's two most populous countries, China and India, where there is little pill use.

OCs are the top modern method among married women in 78 of 150 countries with available data and, if China and India are omitted from the world estimate, the most widely used contraceptive method overall. Outside China and India about 12% of married women use the pill. By comparison, 9.5% rely on female sterilization, and almost as many use traditional or folk methods. About 9% use IUDs. (Table 2 presents OC use data with and without China and India.)

**Table 1. Estimated Ever Use of Oral Contraceptives Among Married and Sexually Active Unmarried Women Ages 15–49, by Region, 2000**

Region	Married Women			Sexually Active Unmarried Women		
	% Ever Using OCs	% Ever Using Any Method	% of Ever Users of Family Planning Ever Using OCs	% Ever Using OCs	% Ever Using Any Method	% of Ever Users of Family Planning Ever Using OCs
<b>ASIA*</b>	<b>16.9</b>	<b>56.0</b>	<b>30.1</b>			
East Asia (except China).....	14.2	85.9	16.6			
India.....	5.3	46.9	11.3			
South Central Asia (except India).....	21.8	49.1	44.4			
Southeast Asia.....	38.8	78.5	49.4			
<b>LATIN AMERICA &amp; CARIBBEAN</b>	<b>55.1</b>	<b>84.0</b>	<b>65.5</b>	<b>54.5</b>	<b>88.6</b>	<b>61.5</b>
Caribbean.....	42.7	69.8	61.1	48.0	59.1	81.2
Central America.....	41.4	76.8	53.8	60.5	89.1	68.0
South America.....	61.8	88.3	70.0	53.4	92.4	57.8
<b>NEAR EAST &amp; NORTH AFRICA</b>	<b>35.7</b>	<b>71.0</b>	<b>50.3</b>			
Near East.....	31.6	76.1	41.6			
North Africa.....	43.3	61.6	70.3			
<b>SUB-SAHARAN AFRICA</b>	<b>14.5</b>	<b>35.6</b>	<b>40.8</b>	<b>23.2</b>	<b>60.8</b>	<b>38.2</b>
Central Africa.....	7.1	39.6	18.1	11.4	67.0	17.0
East Africa.....	19.5	41.4	47.1	19.7	43.8	44.9
Southern Africa.....	48.7	82.9	58.7	35.6	73.0	48.7
West Africa.....	7.4	21.9	33.8	20.9	61.9	33.9
<b>All developing areas except China</b>	<b>23.4</b>	<b>57.8</b>	<b>40.3</b>			
<b>All developing areas except China &amp; India.....</b>	<b>31.6</b>	<b>63.0</b>	<b>50.2</b>			

\*Totals for Asia do not include China, since recent survey data on ever-use are not available. Also, few or no data are available on unmarried women in countries of Asia, Near East and North Africa.

Sources: Demographic and Health Surveys, Reproductive Health Surveys, and US Bureau of the Census International Database

Population Reports



Considering developing countries alone, 6% of married women use the pill—far fewer than use female sterilization, at 21%, and the IUD, at 13%. When China and India are removed from the use estimate, however, OCs become the most popular method in developing countries, used by 10% of married women compared with 9% relying on female sterilization and 8% on traditional methods. IUD use falls to 7%.

In developed countries OCs are the most widely used method. Some 16% of married women use the pill. Condoms and the IUD tie for second place at 14%, while slightly less than 14% of married women use traditional or folk methods.

Worldwide, among sexually active unmarried women, OCs are even more widely used than among married women. In countries with available data 26% of sexually active unmarried women use the pill. Data on current contraceptive use among unmarried women are available in Africa, Eastern

Europe, Latin America, the Caribbean, and most developed nations. OCs are the most popular method among unmarried women in Latin America, North America, and Northern and Western Europe.

Patterns in use of family planning methods vary considerably within and among countries and regions. Differences in availability, access, cost, promotion, program policy, as well as people's preferences, help to explain these differences. Indeed, exceptionally high rates of use for any one method can suggest that access to other methods may be limited.

**Near East and North Africa.** In this region nearly 10 million women use OCs—13% of the region's 74 million married women. Three of every 10 family planning users are pill users. In Algeria, Iran, Kuwait, Morocco, Oman, Qatar, and the United Arab Emirates, OCs are the most widely used method.

**Table 2. Estimated Current Oral Contraceptives Use Among Married and Sexually Active Unmarried Women Ages 15–49, by Region, 2000**

Region	Married Women			Sexually Active Unmarried Women		
	% Using OCs	Number Using OCs (in Millions)	% of Family Planning Users Using OCs	% Using OCs	Number Using OCs (in Millions)	% of Family Planning Users Using OCs
<b>DEVELOPING AREAS</b>						
<b>ASIA*</b> .....	<b>4.5</b>	<b>29.3</b>	<b>7.7</b>			
China.....	3.1	7.6	3.7			
East Asia (except China).....	1.9	0.3	2.6			
India.....	1.2	2.5	2.9			
South Central Asia (except India).....	7.5	6.6	28.9			
Southeast Asia.....	13.5	12.4	23.4			
<b>LATIN AMERICA &amp; CARIBBEAN</b> .....	<b>13.8</b>	<b>11.4</b>	<b>20.3</b>	<b>23.5</b>	<b>3.2</b>	<b>35.0</b>
Caribbean.....	10.4	0.6	17.7	12.3	0.2	22.9
Central America.....	8.4	1.9	13.2	21.6	0.7	40.2
South America.....	16.4	9.0	23.1	25.6	2.4	34.9
<b>NEAR EAST &amp; NORTH AFRICA*</b> .....	<b>13.3</b>	<b>9.8</b>	<b>29.7</b>			
Near East.....	10.6	5.1	23.2			
North Africa.....	18.3	4.7	42.5			
<b>PACIFIC (OCEANIA)</b> .....	<b>5.2</b>	<b>0.1</b>	<b>18.8</b>			
<b>SUB-SAHARAN AFRICA</b> .....	<b>3.6</b>	<b>3.6</b>	<b>23.4</b>	<b>10.4</b>	<b>1.5</b>	<b>24.3</b>
Central Africa.....	0.9	0.1	7.6	4.0	0.1	7.9
East Africa.....	5.3	2.1	30.6	8.1	0.3	27.9
Southern Africa.....	10.5	0.7	19.8	22.3	0.8	38.4
West Africa.....	1.9	0.8	20.8	6.1	0.4	15.6
<b>All developing areas</b> .....	<b>6.0</b>	<b>54.3</b>	<b>11.2</b>			
<b>All developing areas except China &amp; India ...</b>	<b>9.8</b>	<b>44.2</b>	<b>23.1</b>			
<b>DEVELOPED AREAS</b>						
<b>AUSTRALIA &amp; NEW ZEALAND</b> .....	<b>23.4</b>	<b>0.8</b>	<b>30.9</b>	<b>36.1</b>	<b>0.5</b>	<b>65.0</b>
<b>EASTERN EUROPE &amp; CENTRAL ASIA</b> .....	<b>5.8</b>	<b>3.8</b>	<b>9.0</b>	<b>6.5</b>	<b>0.6</b>	<b>13.1</b>
<b>EUROPE</b> .....	<b>30.9</b>	<b>18.4</b>	<b>40.7</b>	<b>44.6</b>	<b>10.2</b>	<b>54.6</b>
North.....	24.3	2.6	30.0	41.6	2.3	58.0
South.....	14.1	3.3	19.4	26.4	1.5	39.6
West.....	49.0	12.5	63.8	55.0	6.4	68.9
<b>NORTH AMERICA</b> .....	<b>16.1</b>	<b>6.5</b>	<b>21.1</b>	<b>35.8</b>	<b>6.4</b>	<b>42.2</b>
<b>All developed areas</b> .....	<b>15.9</b>	<b>29.7</b>	<b>22.5</b>	<b>31.1</b>	<b>17.7</b>	<b>44.0</b>
<b>WORLD</b> .....	<b>7.7</b>	<b>84.0</b>	<b>13.6</b>			

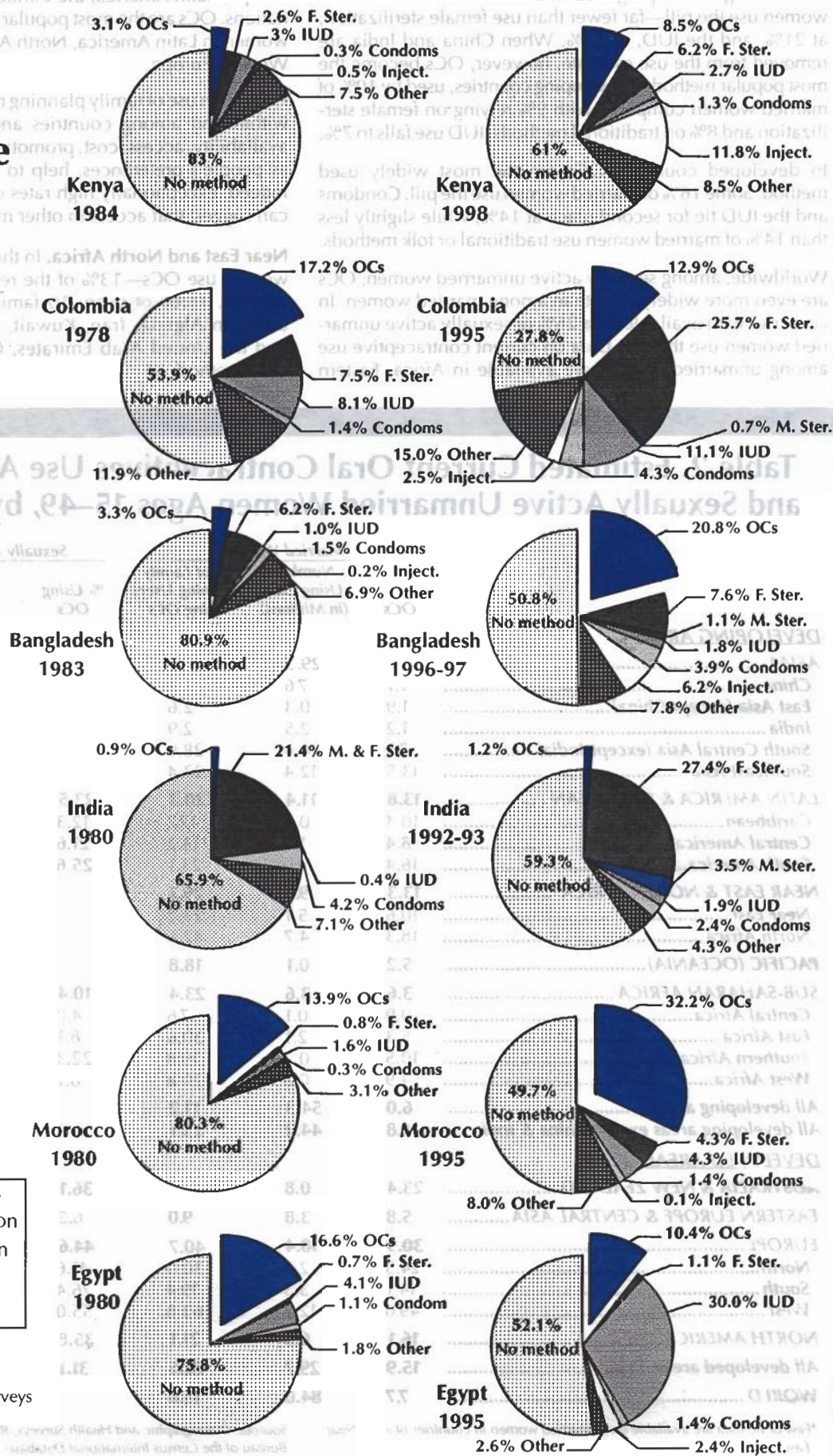
\*Few or no data are available on unmarried women in countries of Asia, Near East and North Africa.

Sources: Demographic and Health Surveys, Reproductive Health Surveys, and U.S. Bureau of the Census International Database

Population Reports



**Figure 1.**  
**Change in**  
**Contraceptive**  
**Method Mix,**  
**Selected**  
**Developing**  
**Countries,**  
**1978–1998**



Source: Demographic and Health Surveys  
 and World Fertility Survey  
**Population Reports**



In Algeria 44% of married women relied on the pill in 1995—the highest level of pill use in the developing world, accounting for 84% of all contraceptive use. Iran and Kuwait also report high levels of pill use, at 23% and 24% of married women. In contrast, levels of OC use are low—4%—in Turkey, where overall contraceptive use is 64%, and in Yemen, where overall use is about 21%.

In Morocco pill use has risen substantially, from 14% of married women in 1980 to 32% in 1995. In Egypt, however, OC use fell from 17% of married women in 1980 to 10% in 1995. In the 1990s many Egyptian women shifted to IUDs (188), which have been more promoted. (See Figure 1.)

**Latin America and the Caribbean.** In Latin America and the Caribbean, OCs are the second most widely used method among married women, following female sterilization. About 14% of married women use the pill—nearly one in every seven married women, or one in every five family planning users.

Some of the world's highest levels of current OC use, as well as ever use, are found in Latin American countries. For example, in Brazil 6 million women use the pill—in numbers fourth in the world after China, Germany, and Indonesia. Some 21% of married women used OCs in 1996, over one-fourth of all Brazilian women using family planning. Brazilian women overwhelmingly use either the pill or female sterilization. Access to the IUD is limited, and a 1994 rating of access to family planning methods found that the condom was readily accessible to less than 80% of couples in Brazil (73).

In some Latin American countries contraceptive use shifted from the 1980s through the mid-1990s. Smaller percentages used OCs as the use of female sterilization and IUDs grew. Overall, OC use rates dropped from one in every six married women in 1987 to one in every seven in 2000. In Colombia, for example, prevalence of OC use fell from 17% of married women in 1978 to 13% in 1995 (see Figure 1). In Mexico OC use declined from 14% in 1982 to 8% in 1995. At the same time, overall contraceptive use increased from 46% to 72% in Colombia and from 48% to 67% in Mexico. Researchers studying Mexican data conclude that the shift from OCs to other methods is occurring because more family planning users are older women choosing IUDs and sterilization once they have had all the children they want (519).

**In Latin America the pill is the most popular way for sexually active unmarried women to avoid pregnancy.** One-fourth of sexually active unmarried women use the pill. Use is highest in Brazil, at 36%.

**Sub-Saharan Africa.** Pill use accounts for about one-quarter of all contraceptive use among both married and unmarried women in sub-Saharan Africa. Overall, about 15% of married women use family planning, and slightly less than 4% use the pill. Among sexually active unmarried women, about 43% use some contraceptive method, and 10% use the pill.

In some African countries levels of OC use are among the world's highest. For example, in Zimbabwe 33% of married women and 32% of sexually active unmarried women were using OCs in 1994. In Zimbabwe access to the pill is generally good, while access to the IUD and to female and male sterilization is considerably more difficult (73). Also, in Reunion 40% of married women use OCs, in Mauritius 21%, and in Botswana and Cape Verde about 18%. Among sexually active unmarried women, about 17% in both Mali and Niger are using the pill, and about 20% in Botswana and South Africa.



*In Bangladesh a village health worker discusses family planning with a client. In this country oral contraceptives have become the most widely used contraceptive, used by about 21% of married women.*

Nevertheless, high levels of pill use are more the exception than the rule in sub-Saharan Africa. In five countries of the region, 1% or less of married women use the pill. In another eight countries use is between 1% and 2%.

**Asia.** In Asia contraceptive prevalence averages 59% of married women of reproductive age, but only 4.5% use the pill. This low percentage for OCs reflects the massive influence of populous China and India. In the most recent surveys only 3% of married women in China and 1% of married women in India reported using the pill. With China and India removed from the estimate, 10% of married women in Asia currently rely on the pill—nearly one-quarter of all family planning users.

Prevalence of OC use is highest in southeast Asia, led by Thailand, where an estimated 27% of married women of reproductive age used OCs in 1993. Despite the low percentage who use the pill, China has more pill users than any other country—about 7.6 million. Indonesia, the world's fourth largest country, has 6.1 million pill users. Few data are available about contraceptive use among unmarried women in Asia.

In a few Asian countries OC use among married women has increased considerably in recent years. In Bangladesh, for example, OCs have become the most widely used contraceptive method, taken by nearly 21% of married women of reproductive age in 1996–97 compared with 3% in 1983 (see Figure 1). Pill use also has grown recently in Sri Lanka and Vietnam.

**Eastern Europe and Central Asia.** In Eastern Europe and Central Asia 65% of married women use family planning, but

*For country-by-country statistics on OC use, see the internet website of the Johns Hopkins Center for Communication Programs at <<http://www.jhuccp.org/pr/a9/a9suptab.stm>>.*



Long-term effectiveness of the pill requires sustained correct use and consistent use. A recent review of 53 reports on contraceptive effectiveness concluded that on average about 7% of OC users are likely to become pregnant in the first three years of use, but the percentage varies depending on whether women take the pill correctly. Among the generally consistent and conscientious users, 3.8% would become pregnant within three years. In contrast, among those who use the pill inconsistently and incorrectly, 7.8% would become pregnant within three years (365).

**Preventing ectopic pregnancy.** Protection against ectopic pregnancy is a benefit of all contraceptive methods, to

Some women forget pills or stop them for a time. This largely accounts for the gap in OC effectiveness between perfect users and typical users. Irregular pill-taking may explain why pregnancy rates than users of injectables, IUDs, or implants. According to Demographic and Health Survey data in 15 developing countries in the 1980s, the pregnancy rate among OC users was about 6 per 100 per year—twice the pregnancy rate among IUD users, at 3 per 100 (312).

Some have speculated that multiphasics might be more likely to allow pregnancy if not used correctly, including taking them out of order (99, 134, 167, 239, 482, 512). Most clinical trials find no difference in effectiveness between multiphasics and constant-dose combined pills, however (124, 142, 371).

Some women forget pills or stop them for a time. This largely accounts for the gap in OC effectiveness between perfect users and typical users. Irregular pill-taking may explain why pregnancy rates than users of injectables, IUDs, or implants. According to Demographic and Health Survey data in 15 developing countries in the 1980s, the pregnancy rate among OC users was about 6 per 100 per year—twice the pregnancy rate among IUD users, at 3 per 100 (312).

Some women forget pills or stop them for a time. This largely accounts for the gap in OC effectiveness between perfect users and typical users. Irregular pill-taking may explain why pregnancy rates than users of injectables, IUDs, or implants. According to Demographic and Health Survey data in 15 developing countries in the 1980s, the pregnancy rate among OC users was about 6 per 100 per year—twice the pregnancy rate among IUD users, at 3 per 100 (312).

Some women forget pills or stop them for a time. This largely accounts for the gap in OC effectiveness between perfect users and typical users. Irregular pill-taking may explain why pregnancy rates than users of injectables, IUDs, or implants. According to Demographic and Health Survey data in 15 developing countries in the 1980s, the pregnancy rate among OC users was about 6 per 100 per year—twice the pregnancy rate among IUD users, at 3 per 100 (312).

## Fertility-Related Benefits

- Effectively prevent unwanted pregnancy, and
- Prevent ectopic pregnancy.

- The greatest number of married users of the pill is in China (7.6 million), followed by Germany (6.8 million), Indonesia (6.1 million), Brazil (6.0 million), Bangladesh (5.7 million), and the United States (5.6 million).
- Nearly one-half of married women in Western Europe use the pill. This amounts to three of every five contraceptive users.
- In the US, an estimated 80% of all women born since 1945 have used the pill at some point in their lives (106).
- OCs are the most popular method among sexually active unmarried women in sub-Saharan Africa and Latin America.
- Some 95% of French women have ever used the pill, contrasted with 4% of Japanese women (356).
- Japan approved the pill for contraceptive use only recently—in September 1999.
- In Canada 7 of every 10 pill users over the age of 35 have been using the pill for more than 10 years (38).

## Facts About Pill Use: Did You Know...?

Oral contraceptives have substantial benefits for women's health. The most important benefit, of course, is highly effective protection against pregnancy. OCs also help prevent ectopic pregnancy (pregnancy outside the uterus) and by reducing menstrual blood loss, OCs lower the risk of iron deficiency anemia. In addition, they help to protect women from epithelial ovarian cancer and endometrial cancer and also may reduce the risks of bone density loss, ovarian cysts, benign breast disease, and colorectal cancer.

## Benefits of Oral Contraceptives

Some of the highest levels of pill use in the world are among sexually active unmarried women in developed countries. Outside Eastern Europe and Central Asia, 36% of sexually active unmarried women in developed countries use the pill. Some 45% in Europe use the pill; in North America, 36%.

Other regions, in most developed countries the majority of married women rely on either the pill or female sterilization. In developed regions outside Eastern Europe and Central Asia, the pill ranks first, used by 21% of married women. In Western Europe half of all married women are pill users. In North America female sterilization is the choice of 24% of married women. The pill ranks second at 16%.

Japan reports the world's lowest rate of OC use. In 1994, when the most recent survey was taken, less than 0.5% of married women relied on the pill. Low-dose OCs were approved for contraceptive use in Japan only in September 1999. Before this date medium- and high-dose pills were available but only to treat menstrual disorders (276).

Among sexually active unmarried women in the region, just 6.5% use the pill, while larger percentages rely on condoms or traditional methods.

only about 6% use the pill. IUDs, traditional methods, and condoms are more widely used. In 8 of 14 countries surveyed in the 1990s, levels of OC use were 5% or lower. Hungary is an exception; some 33% of married women use the pill. OC use is lowest in the Central Asian Republics. Among sexually active unmarried women in the region, just 6.5% use the pill, while larger percentages rely on condoms or traditional methods.



varying degrees. Because they consistently stop ovulation, all combined OCs very effectively prevent ectopic pregnancies (117, 336). Ectopic pregnancy, which occurs when a fertilized ovum develops outside the uterine cavity, can be life-threatening (181). Ectopic pregnancy is fairly common. One US study found that ectopic pregnancy was the reason for 1 in every 13 emergency room visits during the first trimester of pregnancy (446). In the US ectopic pregnancy is the leading cause of pregnancy-related death in the first trimester. In 1992 ectopic pregnancies accounted for 2% of reported pregnancies and 9% of all pregnancy-related deaths in the US (478).

## Menstrual Benefits

The menstrual benefits of OCs include:

- Less iron deficiency anemia, due to lighter menstrual bleeding,
- More regular menstrual cycles,
- Less dysmenorrhea, and
- Less severe premenstrual symptoms.

**Less iron deficiency anemia.** Because their menstrual flow is reduced, OC users may lose only one-third to one-half the blood iron that other women lose during menstruation. For example, a 1992 Danish study found that women using or having used the pill had significantly higher blood iron levels than nonusers and that iron levels increased with the number of years of pill use (307). Studies in Chile (343) and Egypt (401) also have found higher iron levels in OC users than in nonusers. Taking the iron-containing pills packaged as placebos in some brands of 28-day pill packets also may help. A study of Mexican women with anemia found that both hemoglobin and serum iron levels increased significantly after one year of OC cycles consisting of active combined pills for 21 days followed by the iron-containing pills for 7 days (387).

**Because of higher blood iron levels,** OC users are less likely than nonusers to develop iron deficiency anemia (147, 328, 466). Also, by preventing unwanted pregnancies, OCs—like other contraceptives—prevent anemia associated with pregnancy (484). In developing countries anemia is a serious health problem among women, many of whom suffer from inadequate diets, parasitic infections, and the strain of repeated pregnancies. As many as half of women of reproductive age in developing countries may have subnormal levels of hemoglobin, the iron-containing pigment of red blood cells (532, 536).

Some 60% to 80% of women who use OCs bleed less heavily during menstruation than before starting OCs, and on average OC users lose 50% to 60% as much blood per cycle as other women (147, 260, 302, 328, 382, 433, 438). A 1992 Swedish study found that a low-dose OC, containing 30 µg ethinyl estradiol and 0.15 mg desogestrel, reduced menstrual blood loss to 56% of previous levels (260).

**More regular menstrual cycles.** Oral contraceptives generally improve menstrual patterns (179). For example, a UK study of 2,115 women ages 18 to 49 found that most OC users had shorter, lighter periods that occurred at more regular intervals (49). Only 7% of OC users reported irregular periods, compared with 10% of IUD users, 11% of women relying on female sterilization, and 12% of women using other methods or none. The Oxford University/Family Planning Association (Oxford/FPA) cohort study found that, compared with nonusers, OC users or recent OC users (within the previous 12 months) were two-thirds as likely to be referred to a hospital for treatment for irregular periods (495).



This Egyptian poster reminds pill users, "Don't forget to take a pill every day. If you forget, take it with the pill of the following day."

**Less dysmenorrhea.** OCs are highly effective in relieving dysmenorrhea—pelvic pain during menstruation, often accompanied by nausea, vomiting, and diarrhea (113). About half of all women experience dysmenorrhea at some time in their lives, and for about 10% the discomfort is severe enough to interfere with daily life (105, 227).

OCs are a standard treatment for dysmenorrhea (50, 189). A 1990 Swedish study found that users of both monophasic and triphasic low-dose OCs had less severe dysmenorrhea than nonusers (309). Combined OCs appear to be more effective than progestin-only pills at reducing dysmenorrhea (68).

**Less severe premenstrual symptoms.** Several studies have found that premenstrual symptoms are less severe among OC users than among other women (20, 100, 166, 253, 311, 341, 427). Differences in defining and measuring symptoms, however, make it difficult to compare the effects of different formulations (11, 294, 308, 309). Premenstrual syndrome, a condition caused by natural hormonal changes, begins at the middle of the menstrual cycle and tends to intensify in the last seven days before menstruation. Multiple physical and/or emotional symptoms characterize premenstrual syndrome, such as headache, fatigue, acne, backache, breast soreness, changes in sexual desire, nervousness, difficulty concentrating, irritability, anxiety, and depression. Symptoms subside when a woman begins to menstruate. Most women experience noticeable premenstrual symptoms at some time; 10% or less report severe discomfort (50, 225).

## Protection from Some Cancers

Oral contraceptives help to protect women from two cancers of the reproductive organs:

- Endometrial cancer (cancer of the lining of the uterus) and
- Epithelial ovarian cancer.

Studies in the UK and the US suggest that these cancers are about half as common among users of OCs as among other women (59, 196, 210, 234, 236, 375, 516).

Combined OCs probably help protect against these cancers by reducing the rate of cell division in the endometrial lining and the ovaries. In the case of the uterine endometrium, the





Preventing pregnancy offers women control over their lives, as this poster from the Ghanaian social marketing program notes. Oral contraceptives have other benefits, such as preventing some cancers and making menstrual cycles more regular.

progestin component in the pill is thought to counteract the effects of estrogen, which would otherwise encourage cell division. OCs may protect against ovarian cancer by reducing gonadotropin production by the pituitary gland, thus reducing the effects of gonadotropin stimulation of the surface cells of the ovaries (62, 359).

**Endometrial cancer.** Even as little as one year's use of combined OCs cuts the risk of endometrial cancer substantially, and protection lasts long after women stop using OCs. A combined analysis of eight case-control studies and two cohort studies found that longer use significantly increased protection (409, 535). One year of OC use reduced risk to 77% of that among nonusers, 2 years to 62%, 4 years to 49%, 8 years to 36%, and 12 years to 30%. Earlier studies reported protection persisting from 3 to 10 years (195, 210, 234, 516.)

It is uncertain whether the degree of protection against endometrial cancer varies with estrogen and/or progestin dose. The 1985 US Centers for Disease Control's Cancer and Steroid Hormone (CASH) study found no relationship between progestin dose and the degree of protection (58). Although the number of women using any one formulation in the CASH study was too small to allow an analysis by formulation, both high- and low-dose pills had a protective effect. In contrast, a 1991 WHO study suggested that protection was greater for users of formulations containing high doses of progestins (393, 460). Although there are no studies on whether progestin-only OCs protect against endometrial cancer, studies of the effects of progestins on the endometrium suggest that it is progestin rather than estrogen that confers the protective effect (243, 297, 360). Moreover, a 1991 WHO study of the progestin-only injectable contraceptive depot medroxyprogesterone acetate (DMPA) found that it protected against endometrial cancer as well as combined OCs (461). Therefore progestin-only OCs may have at least some protective effect (297).

**Epithelial ovarian cancer.** Combined OCs help protect against epithelial ovarian cancer (12, 59, 62, 92, 200, 299, 325, 391, 474, 515, 524). This finding from the large 1985 CASH study and many earlier, smaller studies has been confirmed over the past decade (180, 345, 386, 390).

In the CASH study women using OCs for 10 years or more reduced their risk of ovarian cancer to 20% of that among nonusers. The CASH study also found that protection against epithelial ovarian cancer persists long after women stop using OCs. Even women who had stopped using OCs 15 or more years earlier faced just half the risk that never-users faced. Each of the 11 pill formulations studied offered similar protection, whether the formulation was high- or low-dose (59).

The protective effect of OCs against epithelial ovarian cancer may grow in importance in the coming years. All studies to date have focused on women younger than 55, since most OC users and former users are in this age group. Ovarian cancer is more common in women over age 60, however. Since the protective effect of OC use apparently persists for many years, widespread OC use may eventually result in a decline in the incidence of this frequently fatal disease. Epithelial ovarian cancer is by far the most common type of ovarian cancer (59).

## Other Possible Health Benefits

Use of OCs also may lower the risks of:

- Loss of bone density,
- Ovarian cysts,
- Benign breast disease, and
- Colorectal cancer.

**Bone density.** Several studies suggest that OC use may stabilize or even increase bone density (127, 164, 247, 250, 278, 416). A retrospective study of 2,297 women, 76% of whom were postmenopausal, found that women with high bone density were significantly more likely to have used OCs than were women with low bone density. Bone mineral density increased with duration of use (247). Clinical studies suggest that the bone mass benefits of OC use are related to the estrogen dose, with estrogen doses below 15  $\mu\text{g}$  resulting in a net loss of bone mass and doses greater than 25  $\mu\text{g}$  resulting in a net gain (109). Therefore some very low-dose pills may not help prevent loss of bone density.

It has not been demonstrated that the effect of OCs on bone density makes a practical difference. Neither of the two major British cohort studies, the Royal College of General Practitioners study or the Oxford/FPA study, found that pill use helped to protect premenopausal women from bone fractures (87, 492).

**Ovarian cysts.** Several early studies indicated that high-dose OCs—those containing 50  $\mu\text{g}$  or more of estrogen—protect women from functional ovarian cysts (334, 397, 493). The Oxford/FPA cohort study found that the risk of follicular ovarian cysts in current OC users was about half that in users of nonhormonal methods. The protection from corpus luteum cysts was even greater. Users of combined OCs faced about one-fifth the risk that other women faced (493). Low-dose combined and multiphasic OCs, even though they prevent ovulation effectively, may permit some follicular development and thus offer less protection against cysts (155, 436) or perhaps none at all (74, 207, 258).



**Benign breast disease.** Studies of women using older, higher-dose formulations found that OC use protected against fibroadenoma and fibrocystic breast disease. OC users had from one-quarter to one-half the risk of nonusers (45, 335, 398).

Protection against benign breast disease may depend on the progestin content of the pill, with more progestin offering more protection. The Oxford/FPA cohort study compared women using pills with the same amount of estrogen but with different amounts of the same progestin. Women using pills containing 2.5 or 3.0 mg of the progestin norethindrone acetate had half the incidence of fibrocystic breast disease as women who used pills with 1.0 mg norethindrone acetate. Also, protection increased with length of pill use (45). Since most OCs now in use contain lower amounts of progestin than in this study, they may offer less protection against benign breast disease (29, 265).

**Colorectal cancer.** Some studies have found that OC use reduces the risk of colorectal cancer (26, 135, 148, 293, 364). The largest case-control study to date found that women who had ever used OCs reduced their risk of colorectal cancer to 60% of that of nonusers and that OC use for over two years reduced risk to 50% (135). Other studies, however, have found no protective effect (252, 468, 514). Colorectal cancer is the fifth most common cancer among women worldwide (348, 542).

## Health Risks of Oral Contraceptives

Modern oral contraceptives are safe for the great majority of women. The health risks of using OCs are much less than the risks of pregnancy and childbearing for almost all women, especially in countries with high maternal mortality rates. Even where maternal mortality is low, pill use is safer than childbearing except for older women who smoke or have high blood pressure (130, 332, 337). Today, with the lower doses in modern pills, the risks of a number of medical conditions appear to be lower than in the past. Also, recent large studies have made it possible to assess the health risks of long-term OC use more accurately and to better identify the groups most likely to experience them.

A major finding of the last decade is the increased risk of heart attack and stroke for older OC users with hypertension. For OC users who do not smoke and do not have high blood pressure, however, the low doses in today's pills appear to minimize these risks.

The major established health risks of OCs are certain circulatory system diseases, particularly heart attack, stroke, and venous thromboembolism. Other health risks include gallbladder disease in women already susceptible to it and rare noncancerous liver tumors. In addition, users and providers of OCs should be aware of possible interactions between OCs and other drugs that might make OCs less effective or modify the effects of the other drugs.

### Circulatory System Diseases

Evidence that combined OCs increased the risks of venous thromboembolism, heart attack, and stroke first appeared in the mid-1970s. The research involved OCs that contained

50 µg or more of estrogen along with a progestin. These circulatory system diseases are rare in young women. Except for thromboembolism, increased risks among OC users were concentrated in older women who smoked or had other risk factors such as high blood pressure. To reduce the risk of circulatory system disease, the second- and third-generation OCs contain less estrogen. Third-generation OCs are pills containing an estrogen dose of less than 50 µg and either of two newer progestins—desogestrel or gestodene. All other pills containing less than 50 µg of estrogen are considered second-generation OCs (except those containing cyproterone acetate or norgestimate, which are difficult progestins to categorize).

**Heart attack.** Ischemic heart disease results from an impediment to circulation that deprives the heart of adequate blood supply. Myocardial infarction—heart attack—is the resulting death of heart muscle cells. Ischemic heart disease can develop gradually from atherosclerosis, in which deposits on the walls of coronary arteries restrict blood flow to the heart muscle, or it can result from a thrombus, or clot, that suddenly blocks a coronary artery. Myocardial infarction is rare in young women who do not smoke or have other clinical risk factors (122, 463, 540).

**Perle LD**  
LOW DOSE CONTRACEPTIVE PILLS

- ✓ Reduces fear of unplanned pregnancy
- ✓ Reduces risk of side effects

Perle LD is one of the high quality contraceptive products available in the Personal Choice programme.

**Perle LD**  
LOW DOSE ORAL CONTRACEPTIVES

Distributed in Jamaica by  
**medi-grace.**  
Committed Service for better Health Care  
A Member of the One-Kennedy Group  
221 Eastwood Park Road, Kingston 16, Jamaica, W.I.

Jamaican National Family Planning Board

Modern oral contraceptives are safe for the great majority of women. The health risks of using OCs are much less than the risks of pregnancy and childbearing for almost all women, especially in countries with high maternal mortality rates. This Jamaican poster points to high effectiveness and few side effects with low-dose oral contraception.



**Table 3. Myocardial Infarction**

Relative Risk Among Current Users of Oral Contraceptives (OCs) Compared with Nonusers, by History of Hypertension, Smoking Behavior, and Blood Pressure Check Before Starting OCs

	Overall Risk	No History of Hypertension	History of Hypertension	Nonsmokers	Light Smokers <sup>a</sup>	Heavy Smokers <sup>b</sup>
Developing-country hospitals .....	4.8	3.7	15.3	4.5	10.7	22.6
European hospitals .....	5.0	3.9	68.1	4.0	5.0	87.0
	No Blood Pressure Check <sup>c</sup>			Blood Pressure Check <sup>c</sup>		
	Nonsmokers	Smokers		Nonsmokers	Smokers	
Developing-country hospitals .....	9.6	31.0		1.1	9.1	
European hospitals .....	16.4	71.4		1.1	26.6	

<sup>a</sup>Light smoker = less than 10 cigarettes per day

<sup>b</sup>Heavy smoker = 10 or more cigarettes per day

<sup>c</sup>Among women with no history of hypertension other than that associated with pregnancy, diabetes, rheumatic heart disease, or abnormal blood lipids.

Sources: WHO 1997 (539, 540)

Population Reports

**Table 4. Ischemic Stroke**

Relative Risk Among Current Users of Oral Contraceptives (OCs) Compared with Nonusers, by History of Hypertension, Smoking Behavior, and Blood Pressure Check Before Starting OCs

	Overall Risk	No History of Hypertension	History of Hypertension	Nonsmokers	Smokers	
Developing-country hospitals .....	2.9	2.7	14.5	2.6	4.8	
European hospitals .....	3.0	2.7	10.7	2.1	7.2	
	No Blood Pressure Check			Blood Pressure Check		
	Under Age 35	Age 35 and Over	All Ages	Under Age 35	Age 35 and Over	All Ages
Developing-country hospitals .....	2.6	5.9	3.8	1.6	2.7	1.9
European hospitals .....	2.8	5.9	3.9	2.2	2.5	2.3

Sources: Poulter 1996 (367), WHO 1997 (540)

Population Reports

Using OCs may somewhat increase heart attack risk, but risk is largely limited to older women who smoke or have high blood pressure. Early case-control studies found that the risk of myocardial infarction (heart attack) in current OC users was two to four times greater than in nonusers (286, 287, 288, 290, 431). Recent studies suggest risk less than twice that of nonusers. For example, a recent US case-control study found that OC use increased risk by about 1.7 times. In this study an estimated 5% of myocardial infarction cases were attributable to current OC use, the equivalent of less than three additional heart attacks per 1 million US women in one year of OC use (425). Two other recent case-control studies, one in the US (389) and one in the UK (465), found no significantly increased risk among either current or past OC users. The findings of lower risk may be attributable to use of lower-dose OCs and perhaps also to better screening of potential pill users for risk factors such as smoking (463).

Combining OC use with other risk factors for heart disease, particularly smoking, hypertension, and long-term or uncontrolled diabetes, raises the risk of myocardial infarction substantially (288, 353, 463). Relative risk\* increases considerably in pill users who smoke (95, 163, 353, 388, 415, 463). Between 1989 and 1993 the World Health Organization (WHO) conducted a large case-control study of cardiovascular disease and hormonal contraceptives in 21 hospitals in Europe and in developing countries of Africa, Asia, and Latin America. OC users with histories of hypertension or who were heavy smokers were at a much greater risk of heart attack relative to OC users without either of these risk factors (see Table 3).

The WHO study found the relative risk of heart attack associated with OC use was higher among women who had not had their blood pressure checked before starting to use OCs—presumably because some of them did have high blood pressure, whereas the group of OC users who had been screened excluded most women with high blood pressure (539).

Among nonsmoking OC users who had their blood pressure checked before starting OCs and had no other risk factors for heart attack, there was no appreciable increase in risk in either European or developing countries (539, 540). The researchers conclude that:

*Women who do not smoke, who have their blood pressure checked, and who do not have hypertension or diabetes are at no increased risk of myocardial infarction if they use combined oral contraceptives, regardless of age. There is no increase in the risk of myocardial infarction with increasing duration of use of combined oral contraceptives. There is no increase in the relative risk of myocardial infarction in past users of oral contraceptives. These conclusions appear to apply equally to women in developed and developing countries. (540)*

\*Relative risk is a measure of how much a particular factor influences the risk of a specified outcome. For example, a relative risk of 2 associated with a factor means that people with the factor face twice the risk of having a specified outcome that people without the factor have. A relative risk of 0.5 means that people with the factor have half the risk of the specified outcome that people without the factor have (a protective effect).



Recent studies have suggested no increased risk of myocardial infarction among users of third-generation OCs with no other risk factors (222, 268, 270). The rarity of myocardial infarction in women of reproductive age, the large number of different OC formulations, and the differing geographic distributions of users of specific formulations will make it difficult to compare various formulations in detail, however (353).

Recent studies—and most older ones—have found that heart attack risk does not increase with duration of OC use. Also, risk does not persist after a woman stops using OCs (3, 10, 95, 104, 288, 289, 375, 415, 425, 431, 442, 443, 465, 539).

**Stroke.** Cerebrovascular disease occurs in two forms: thrombotic stroke and hemorrhagic stroke. Thrombotic stroke, also called occlusive or ischemic stroke, occurs when the flow of blood in the brain is blocked. Hemorrhagic stroke occurs when a blood vessel in the brain ruptures. The most common stroke in women of reproductive age is subarachnoid hemorrhage, in which blood from the ruptured vessel enters the space below the brain's arachnoid membrane and spreads through cerebrospinal fluid passageways. Hemorrhagic stroke is more likely to be fatal than ischemic stroke (281, 282, 441).

**Studies with low-dose OCs in the 1980s and 1990s suggest less overall risk of stroke than did earlier studies (464).** The first studies of the health risks of OC use, conducted in the 1960s and 1970s, suggested about a fivefold greater risk of any type of stroke among OC users than among nonusers (81, 213, 224, 263, 264, 355, 375, 441, 490). Now, based on the results of a multi-center WHO study (367) and other recent studies (192, 354, 412), the estimated risk of ischemic stroke among OC users is about 2.5 times greater than the risk among nonusers (131). The more recent studies provide more information on ischemic stroke than on hemorrhagic stroke.

**Lower doses appear to have reduced the risk. For example, in the Oxford/FPA cohort study, the relative risk of stroke for OC users appeared to drop as the study progressed.** In 1984 the study reported relative risks of 1.5 to 2.0 for subarachnoid hemorrhage and 2.3 to 3.2 for other types of stroke among OC users compared with nonusers (497), down from 5.0 for all types in 1976 (490).

**The multicenter WHO study—the largest case-control study of stroke and OCs by far—found an overall relative risk of ischemic stroke of about 3 among OC users.** As with heart attacks, other risk factors make a big difference to the risk of OC use (see Table 4). Current OC users who did not smoke, had their blood pressure checked, and did not have high blood pressure were at 1.5 times greater risk than nonusers. In contrast, OC users who smoked faced a higher risk—about two times greater than among nonsmoking OC users in the developing countries studied and about 3.5 times greater in Europe. Current OC users with a history of hypertension faced the greatest risk—about five and four times greater than for other OC users. As in the WHO study of heart attack, the risk of ischemic stroke was lower among women who re-

## What's smoking got to do with the pill?



*Smoking increases the risk of heart attack and stroke especially for older women who use oral contraceptives. This US poster warns of the risk and urges pill users not to smoke.*

ported having their blood pressure checked before starting OCs than among those who did not (367).

The WHO study produced conflicting findings on the relationship between dosage and ischemic stroke risk. In Europe lower doses meant lower risks, while in the developing countries the pattern was reversed. The researchers suggest that the opposing patterns reflect different levels of other risk factors for ischemic stroke. In both Europe and the developing countries, however, risk did not rise significantly with continuing OC use, and elevated risk did not appear to persist after women stopped using OCs (367).

Migraine headaches have been linked to a twofold or greater increased risk of ischemic stroke. Several studies have found that OC users with a history of migraine are two to four times more likely to have an ischemic stroke than women with a history of migraine who do not use OCs (69, 272, 273, 274, 411, 475). For example, a case-control study conducted in European hospitals from the WHO study of cardiovascular disease and hormonal contraceptives found that, compared with women not using OCs and having no history of migraine, ischemic stroke was 6.6 times more likely among OC users with a history of migraine, and 2.3 times more likely among nonusers with a history of migraine (69). Studies suggest risk is greater among women who have severe migraine headaches with "aura"—focal neurologic symptoms such as blurred vision, temporary loss of vision, seeing flashing lights or zigzag lines, or trouble speaking or moving (61, 69, 411, 475). The recent studies (61, 69, 273, 475) led a March 2000 meeting of experts convened by WHO to recommend that a woman who has migraine headaches with focal neurologic symptoms should not start combined OCs. The group recommended that a woman age 35 or older should choose another method if possible if she has migraine headaches even without focal neurologic symptoms. Mild or severe headaches that are not migrainous do not rule out OC use (557).

**For hemorrhagic stroke, the WHO study found a slightly increased risk among OC users in general (see Table 5). The**



# Table 5. Hemorrhagic Stroke

Relative Risk Among Current Users of Oral Contraceptives Compared with Nonusers, by History of Hypertension and by Smoking Behavior and Age

	Overall Risk		No History of Hypertension		History of Hypertension	
<i>Developing-country hospitals .....</i>	1.8		1.4		14.3	
<i>European hospitals .....</i>	1.4		1.1		10.3	
	Nonsmokers			Smokers		
	Under Age 35	Age 35 and Over	All Ages	Under Age 35	Age 35 and Over	All Ages
<i>Developing-country hospitals .....</i>	0.9	2.3	1.5	2.6	5.4	3.7
<i>European hospitals .....</i>	0.7	2.4	1.2	2.7	3.9	3.1
Sources: WHO 1996, 1997 (537, 540)						
Population Reports						

Sources: WHO 1996, 1997 (537, 540)

Population Reports

difference was statistically significant in developing countries but not in the European countries. In both developing and European countries, current OC users age 35 or over had a significantly increased risk of hemorrhagic stroke, with relative risks of 2.5 and 2.2, respectively, compared with nonusers of OCs. The relative risk among current OC users who smoked was three to four times that of nonusers who did not smoke. Also, current users with a history of hypertension faced a substantially higher relative risk than nonusers with no such history. As with ischemic stroke, the duration of OC use did not affect the risk of hemorrhagic stroke, and the elevated risk did not persist after OC use ended. Risk did not vary with estrogen dose or with progestin dose or type (537, 540).

Because, in combination, hypertension and OC use increased the risk of stroke and myocardial infarction far more than would either risk factor alone, WHO medical eligibility criteria for OC use were recently revised to recommend that women who know that they have high blood pressure—systolic pressure of 140 mm Hg or higher and/or diastolic pressure of 90 or higher—or, where blood pressure cannot be evaluated, who have a history of hypertension should choose another contraceptive method (557). (Blood pressure must be properly taken, and one reading is not enough to diagnose high blood pressure.)

In areas where medical services are limited, blood pressure checks for OC users may be impractical. In these service areas, maternal mortality and morbidity tend to be greater risks than any risks associated with OC use (540).

In any case, the benefit of screening potential combined OC users for high blood pressure and withholding OCs from women with high blood pressure would not be substantial if hypertension itself cannot be treated. A recent analysis conducted for WHO pointed out that this screening would prevent only about 10% of stroke and heart attack cases attributable to OC use. In particular, screening women under age 35 for high blood pressure would not prevent an appreciable number of cardiovascular disease cases or deaths attributable to OC use. At the same time, "false positive" diagnoses of hypertension would needlessly prevent some women from using OCs (556).

From a public health perspective, the impact of cardiovascular disease attributable to OC use is slight, particularly since most OC users are young and do not have other risk factors for cardiovascular disease. The analysis for WHO points out that the additional number of cardiovascular disease cases and deaths among OC users depends greatly on age. For example, among one million OC users under age 35, 20% of whom smoke, fewer than 20 deaths annually would be due

to OC use. By comparison, among one million OC users over age 35, 20% of whom smoke, 24 to 96 deaths annually would be attributable to OC use, depending on the region (556).

**Thromboembolism.** Thromboembolism is an obstruction of a blood vessel by a blood clot. The most common thromboembolic disorder in OC users—known as venous thromboembolism (VTE), or deep vein thrombosis—involves clots that form in veins deep in the leg. These clots sometimes circulate to the lungs, where they become potentially fatal pulmonary embolisms. A multinational study by WHO, conducted from 1989 to 1993 (366), and three smaller studies in the mid-1990s (34, 221, 440) found that modern low-dose OCs pose less risk of thromboembolism than indicated by earlier studies that involved mostly first-generation pills.

The new case-control studies reported a risk of VTE about three times greater among users of second-generation OCs than among women not using OCs and about six times greater among users of third-generation OCs containing desogestrel and gestodene (131). There is debate about whether the difference in risk between second- and third-generation pills is real or due to bias in the studies (88, 131, 132, 194, 223, 267, 269, 275, 368, 440, 447, 503, 540, 554).

When the findings were released in 1995, they caused a "pill scare" in the news media of the UK and other European countries where third-generation OCs are most widely used. Responding to the publicity, many women switched to other OCs or stopped taking pills altogether. In the months following, the number of unintended pregnancies and abortions increased substantially (15, 75, 76, 118, 218, 257, 376, 528).

The estimated risk of VTE is low with all modern low-dose OCs—including those containing desogestrel and gestodene—and all low-dose OCs pose less risk of VTE than previous higher-dose formulations. For users of high-dose OCs, early studies suggested that about 80 cases of VTE per 100,000 women per year could be attributed to OC use (197, 221, 358, 441). By comparison, recent studies estimate that the annual number of VTE cases attributable to second-generation OCs ranges from about 6.5 cases per 100,000 women per year at ages 20 to 24 to 12 cases per 100,000 per year at ages 40 to 44. The number attributable to third-generation OCs ranges from about 16 cases per 100,000 at ages 20 to 24 to 30 cases per 100,000 at ages 40 to 44 (131). VTE risk associated with pregnancy is about 60 cases per 100,000 pregnancies (86).

The risk of death from VTE is slight. Worldwide, among women not using OCs, an estimated 0.6 to 1.2 deaths per million

(Text continues on page 25.)



# Emergency Contraceptive Pills

More and more women and their health care providers are becoming aware that some oral contraceptive pills, or the same hormones used in these OCs, can serve as emergency contraception. That is, they can help to prevent pregnancy when taken after unprotected intercourse. Emergency contraceptive pills (ECPs) offer a chance to avoid pregnancy to women who did not or could not use contraception or who suspect that their regular method failed. Both progestin-only and combined estrogen-progestin formulations are effective. According to recent research, progestin-only ECPs are more effective and cause less nausea and vomiting.

ECPs are safe and easy to use. Virtually all women can use them, even women who have medical conditions that rule out ongoing use of OCs. Pills from an ordinary OC pill packet can be used for emergency contraception, so long as the pills contain the progestin levonorgestrel, or norgestrel. Thus in effect ECPs are available wherever these combined oral contraceptive pills or progestin-only pills are available. ECPs are not as effective as correct and consistent use of most other modern contraceptive methods, however, and they are more likely to cause nausea and vomiting than OCs taken daily. Therefore ECPs should not be used regularly as a substitute for ongoing contraception.

## Long History, New Attention

The use of combined oral contraceptive pills for emergency contraception is not new. Sometimes referred to as the Yuzpe regimen after its developer, Canadian researcher Albert Yuzpe (549, 550), combined pills have been used for emergency contraception safely and effectively—but not widely—for over 30 years.

Now ECPs are emerging from their status as a “well-kept secret” (204). As a part of efforts to make emergency contraception better known and more available, in April 1995, 24 medical experts from around the world met in Bellagio, Italy. They made recommendations on research, policy, information, and communication intended to increase access to emergency contraception (129). Later that year seven organizations involved in women’s reproductive health formed the Consortium for Emergency Contraception. The Consortium advocates worldwide development and distribution of dedicated emergency contraceptive pills—packaged especially for emergency contraception—and offers a variety of informational materials (85) (see p. 24). In December 1995 the World Health Organization (WHO) added the Yuzpe regimen of combined OCs for emergency contraception to the WHO model list of essential drugs (541). The US Food and Drug Administration (USFDA) declared in 1997 that six brands of combined oral contraceptives could be used

*The US Food and Drug Administration declared in 1997 that six brands of combined oral contraceptives could be used safely and effectively as ECPs.*

Just had sex?  
Worried about pregnancy?



You have 3 DAYS to act.

Emergency contraceptive pills can help prevent pregnancy if taken within 3 days after unprotected sex.

Ask your health care provider for more information or call the Emergency Contraception Hotline

**1-888-NOT-2-LATE**  
<http://opr.princeton.edu/ec/>

PHOTO: JAMES H. HARRIS

*In several countries telephone hotlines offer ready information about emergency contraception and where to obtain it.*



safely and effectively as ECPs (481). Several more have been approved since. In 1998 USFDA approved *Preven*, the first estrogen-progestin regimen marketed in the US specifically as ECPs. USFDA approval for a two-pill progestin-only regimen, *Plan B*, came in 1999; it had already been approved in 39 other countries.

ECPs are becoming increasingly available around the world. In some countries combined and progestin-only OCs are packaged specifically for use as emergency contraception. These packages contain the appropriate dosage along with instructions for the user and the provider. In some places ECPs are sold over-the-counter or with the referral of a pharmacist, while other places require a physician's prescription.

## Effectiveness of ECPs

Progestin-only ECPs may be more effective than combined pills. ECPs containing estrogen probably prevent at least three-fourths of pregnancies that would have otherwise occurred (472). Typically, if 100 women had unprotected sex once during the second or third week of their menstrual cycles, 8 of them would become pregnant. If these same women all used ECPs containing estrogen, however, only two would become pregnant (518).

A recent WHO study found that women using progestin-only ECPs were one-third as likely to become pregnant as women using combined ECPs (453). Thus, if the same 100 women used progestin-only ECPs, only 1 would become pregnant. This is an 88% reduction in the chance of pregnancy compared with not using ECPs (469). It is important to remember that these failure rates are per use and cannot be compared with failure rates for ongoing contraception, including daily use of OCs.

## How Do ECPs Work?

The precise mode of action of ECPs is uncertain and may be related to the time they are used in a woman's cycle (133, 471). It is thought that in the beginning of the cycle they may prevent ovulation just as OCs taken daily would, or they may delay ovulation. After ovulation, they may interfere with fertilization and/or, in theory, prevent implantation of a fertilized egg in the wall of the uterus (175, 448, 518). ECPs are not effective once the process of implantation has begun.

ECPs will not disrupt an established pregnancy. Furthermore, there is no evidence that combined or progestin-only contraceptives harm a developing fetus (133, 160, 518). Studies examining the effects of exposure to oral contraceptives early in pregnancy have not linked such exposure to congenital malformations (40). Only one study has looked specifically at pregnancy outcomes after failed emergency contraception. It found no evidence that ECPs would adversely affect a fetus (60).

ECPs offer no protection against sexually transmitted infections (STIs). When indicated, as in cases of rape, preventive STI treatment should be provided (190).

## Timing of ECP Use

The sooner treatment is started, the better. The first dose should be taken no later than 72 hours after intercourse. The second dose should follow 12 hours after the first dose. A recent study found that, even within the 72-hour period, effectiveness decreased dramatically as time since intercourse increased (453). With each additional 12 hours, the chances of pregnancy increased by almost 50%. Thus ECPs were eight times more effective when begun in the first 12 hours than when begun 60 to 72 hours after intercourse (357).

How effective ECPs would be if started 72 hours or more after intercourse has not been well studied. It is biologically plausible that ECPs would be effective after 72 hours because there are approximately six days between ovulation and implantation (175, 456). Women who request ECPs more than 72 hours after unprotected intercourse may be given pills, but they should be told that pregnancy may already have begun, and therefore ECPs may not be effective (133, 517). For women who request emergency contraception between 72 and 120 hours and are appropriate IUD candidates, a copper IUD may be a better option (517). An international study, conducted by the Population Council and partner clinics, is underway to determine more accurately the effectiveness of ECPs beyond 72 hours. The study also seeks to determine whether pills containing the progestin norethindrone may be used for emergency contraception and whether the second dose is really necessary (370).

## Safety and Side Effects

ECPs are safe for virtually all women, including those who may have health conditions that rule out daily use of OCs. ECPs have not been found to increase the risk of the complications associated with ongoing OC use (85, 123, 456, 486). One study specifically examined the risk of venous thromboembolism—which is associated with continuing use of combined OCs (see p. 16)—and found no increase in risk among ECP users (488). WHO medical eligibility criteria for contraceptive use list no medical conditions that rule out use of ECPs (557).

Women taking ECPs sometimes experience nausea, dizziness, fatigue, headache, heavier or lighter menstrual bleeding, breast tenderness, and/or abdominal pain. These side effects usually subside within a day or two. In the WHO study, about 50% of women using combined ECPs reported nausea compared with 23% of women using progestin-only ECPs. Approximately 20% of women who used combined OCs and 6% of those who used progestin-only pills vomited (453). Antinausea medication containing meclizine hydrochloride can help prevent nausea and vomiting (381). Diphenhydramine hydrochloride and dimenhydrinate also have been recommended (486). Taking the pills with food or milk also may help (133, 541). If a woman vomits within two hours after taking ECPs, she should take another dose. For women who vomit more

(text continued on page 23)



# Emergency Contraceptive Pills

## Questions and Answers

**Q:** What are Emergency Contraceptive Pills (ECPs)?

**A:** ECPs can be taken after unprotected sex to help prevent unintended pregnancy. They contain some of the same hormones as pills used for daily oral contraception. ECPs are sometimes packaged especially for emergency use (dedicated products), or they can be special doses taken out of a regular pill pack.

**Q:** What are reasons to use emergency contraception?

**A:** A woman has had unprotected sex, and she wants to prevent pregnancy. For example:

- ▶ She did not expect to have sex and was not using contraception.
- ▶ Sex was forced.
- ▶ A condom broke or slipped.
- ▶ She ran out of oral contraceptives, started a new packet of pills several days late, or missed three or more active pills in a row, and she did not use condoms or spermicide.
- ▶ She is late for a contraceptive injection—more than two weeks late for depo medroxyprogesterone acetate (*Depo-Provera*), more than one week late for norethindrone enanthate (*Noristerat*), or more than three days late for a monthly injection (such as *Cyclofem* or *Mesigyna*).

In short, any reason that a woman is concerned that she might become pregnant is an appropriate reason.

**Q:** What pills can be used as ECPs?

**A:** Four types of pills can be used. All four types contain the progestin levonorgestrel, or norgestrel:

- ▶ Progestin-only dedicated products,
- ▶ Progestin-only oral contraceptives,
- ▶ Combined oral contraceptives,
- ▶ Combined progestin-estrogen dedicated products (see table on p. 21).

Progestin-only pills are more effective and cause much less nausea and vomiting than combined pills.

**Q:** How effective are ECPs?

**A:** Among 100 women, if each has sex once in the second or third week of her menstrual cycle without using contraception, 8 women are likely to become pregnant. If all 100 women use progestin-only ECPs, only one is likely to become pregnant. If all 100 women use combined OCs for emergency contraception, only two are likely to become pregnant. ECPs are appropriate in emergency situations, but they are not as effective as ongoing use of most modern contraceptives.

**Q:** When should ECPs be taken?

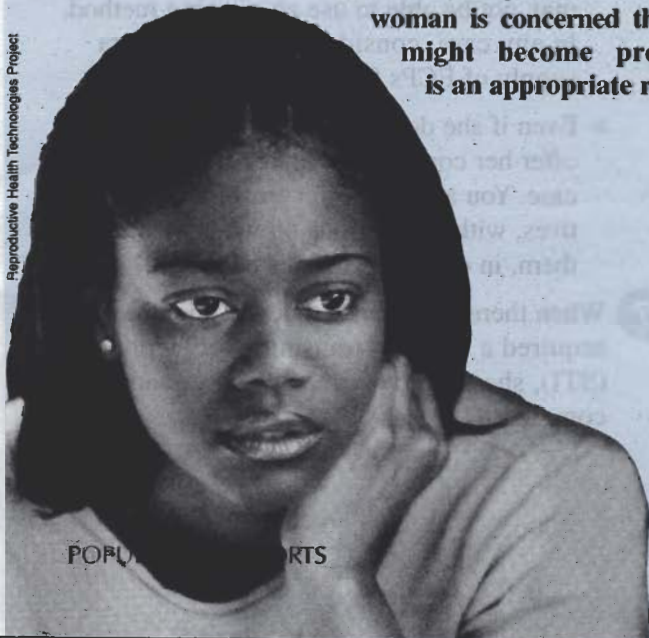
**A:** As soon as possible after unprotected intercourse. The first dose should be taken within 72 hours after intercourse.

**Q:** Are there side effects?

**A:** Yes. Some women have nausea, vomiting, dizziness, headache, breast tenderness, abdominal pain, or a heavier or lighter menstrual period. Nausea and vomiting are most common. With combined pills about 20% of women vomit. With progestin-only pills about 6% vomit. Antinausea medications can help (see p. 22).

**Q:** Do ECPs cause abortion?

**A:** No. ECPs will not disrupt an established pregnancy. They are not effective once the process of implantation has begun.





**Q:** *Do any medical conditions rule out use of ECPs?*

**A:** No medical conditions rule out ECPs. Medical conditions that rule out continuing use of oral contraceptives do not apply to ECPs. Furthermore, there is no suggestion that ECPs increase the risk of complications—such as certain circulatory system diseases—associated with ongoing OC use.

**Q:** *After using ECPs, when can a woman start an ongoing method of contraception?*

**A:** ECPs do not provide continuing protection from pregnancy. Therefore it is important to start an ongoing method of contraception after ECP use. Most methods can be started at once. For example:

- ▶ Condoms and spermicides can be started at once. A woman who wants to start another method later needs to use these methods if she has sex before then.
- ▶ If a woman chooses to use oral contraceptives regularly, she should take the first pill on the next day after she finishes the ECPs. She should also use condoms for the next seven days.
- ▶ A woman who wants an IUD for ongoing contraception can have it inserted within five days of unprotected intercourse in place of taking ECPs.
- ▶ Injectables and implants can be started within seven days after the beginning of the next menstrual cycle. The woman should use condoms until then.
- ▶ Couples who want to use a fertility awareness-based method such as periodic abstinence may need to abstain or use condoms at first and wait one or two cycles until the woman's menstrual cycle becomes regular.

All guidelines also apply to switching to another method after regular use of oral contraceptives.

**Q:** *Where should ECPs be offered?*

**A:** Anywhere that women can get ECPs easily, including chemists' shops and convenience stores, as well as at clinics, emergency rooms, shelters, and private health care providers' offices.

**Q:** *Where should women find out how to use ECPs?*

**A:** Information can come from a pharmacist, a community-based provider, a doctor, a nurse, or from radio, television, newspapers, magazines, package inserts, fliers, telephone recordings, or the Internet.

## Providing ECPs: Suggested Steps for Health Care Providers

*Most important is to see that the woman gets the pills and knows how to take them. If possible, these steps are useful:*

- 1 Help the client feel at ease. Let her know that you understand her needs, you will not judge her behavior, and you will keep her visit confidential.
- 2 Ask when unprotected sex took place. ECPs should be started as soon as possible within 72 hours after unprotected intercourse.
- 3 Give the woman the pills. Explain how to take them (see next page), and point to the pills as you explain. She can take the first dose at once.
- 4 Tell her that, if she vomits within two hours of taking the pills, she may take another dose either by mouth or vaginally.
- 5 Explain and discuss important points about ECPs (see p. 22).
- 6 Discuss the woman's need for ongoing contraception.
  - ▶ If she expects to have sex and wants to avoid pregnancy, it is best if she can choose an ongoing method. In some circumstances—for example, if her partner prevents it—she may not be able to use an ongoing method. In any case, consider offering an extra supply of ECPs for future use.
  - ▶ Even if she does not expect to have sex, offer her condoms or spermicide just in case. You also can offer her oral contraceptives, with instructions on when to start them, in case she changes her mind.
- 7 When there is a chance that she might have acquired a sexually transmitted infection (STI), she should be treated for the most common STIs.



# Emergency Contraceptive Pills

## How to Use ECPs

To use **progestin-only pills** for emergency contraception, a woman must take:

- ▶ A total of 0.75 mg of levonorgestrel within 72 hours after intercourse, and then a second dose of 0.75 mg 12 hours later. (See table below for numbers of pills to take.)

To use **combined OCs** for emergency contraception, a woman should take pills totaling 0.5 mg levonorgestrel (or 1.0 mg norgestrel) and 100 µg ethinyl estradiol within 72 hours after intercourse, and the same dose 12 hours later. For example:

- ▶ Two pills containing 50 µg ethinyl estradiol and 0.25 mg levonorgestrel (or 0.50 mg norgestrel), and then two more of these same pills 12 hours later, OR
- ▶ Usually four "low-dose" combined pills, each containing less than 50 µg of ethinyl estradiol and 0.15 mg levonorgestrel (or 0.30 mg norgestrel), and then four more of these same pills 12 hours later. (A few brands differ; see table below.)

**Dosages for Emergency Contraceptive Pills**

If you are taking...	Number of pills to swallow as soon as possible (within 72 hours)	Number of pills to swallow 12 hours later
<b>Dedicated Progestin-Only ECPs</b>		
Plan B	1 pill	1 pill
Postinor-2	1 pill	1 pill
NorLevo	1 pill	1 pill
<b>Dedicated Combined ECPs</b>		
Preven	2 pills	2 pills
E-Gen-C	2 pills	2 pills
Schering-PC-4	2 pills	2 pills
NeoPrimovlar	2 pills	2 pills
Tetragynon	2 pills	2 pills
Imediat	2 pills	2 pills
<b>Progestin-Only OCs</b>		
Microval	25 pills	25 pills
Ovrette	20 pills	20 pills
<b>Combined OCs</b>		
Alesse	5 pink pills	5 pink pills
Eugynon	2 white pills	2 white pills
Levlen	4 light-orange pills	4 light-orange pills
Levlite	5 pink pills	5 pink pills
Levora	4 white pills	4 white pills
Lo-Femenal	4 white pills	4 white pills
Microgynon	4 yellow pills	4 yellow pills
Lo-Ovral	4 white pills	4 white pills
Nordette	4 light-orange pills	4 light-orange pills
Ovidon	2 pills	2 pills
Ovral	2 white pills	2 white pills
Rigevidon	4 pills	4 pills
Tri-Levlen	4 yellow pills	4 yellow pills
Triphasil	4 yellow pills	4 yellow pills
Tivora	4 pink pills	4 pink pills

Remember that in 28-day pill packs the last 7 pills are not "active" pills and therefore cannot be used for ECP.

Brochures in many languages, available from PATH (see p. 24).



Planinn Rapio  
Pou Ka-Dijans







**The  
sooner  
ECPs are  
started,  
the more  
effective  
they will be.**

## **What Women Should Know About ECPs**

- ▶ The first dose of ECPs should be taken as soon as possible within 72 hours after unprotected intercourse. The second dose should be taken 12 hours later. The sooner ECPs are started, the more effective they will be.
- ▶ ECPs will not protect against other acts of unprotected intercourse later in the menstrual cycle. In fact, ECPs can delay ovulation, so a woman might still get pregnant later in the same cycle. To keep avoiding pregnancy, a woman should start an ongoing method of contraception as soon as possible.
- ▶ ECPs are not as effective as consistent, correct, and ongoing use of OCs or many other modern family planning methods.
- ▶ ECPs do not protect against sexually transmitted infections, including HIV, which causes AIDS.
- ▶ Especially with combined pills, many women have nausea (upset stomach), and some women vomit after taking ECPs. Taking an antinausea medication containing meclizine hydrochloride can help. Antinausea medication should be taken 30 minutes to one hour before the first dose of ECPs and repeated as directed on the package.
- ▶ Taking more than the recommended dosage of ECPs will NOT make ECPs more effective. The extra pills will only cause more nausea.
- ▶ The pills will not make menstruation start immediately. A woman's next period may come a few days earlier or later than expected. This is not harmful and not a reason to worry. She should suspect pregnancy, however, if:
  - Her period is more than one week later than expected, or
  - She has not menstruated within three weeks after treatment, or
  - Her period is unusually light.
- ▶ ECPs are not 100% effective. If they fail, however, the available research suggests that ECPs will not harm the fetus or the course of pregnancy.



than two hours after taking ECPs, another dose is not necessary (380, 517). This advice is based upon medical care providers' best guess rather than scientific data and is, therefore, a topic of debate (456, 517). In cases of severe vomiting, vaginal administration of a second dose of ECPs has been recommended.

Little research has been done on possible drug interactions involving ECPs. Continuing oral contraception is known to be less effective for women taking carbamazepine, paramethadione, phenytoin, or phenobarbital (for seizures), rifampin (for tuberculosis), or griseofulvin (for fungal infections) (see p. 26). Some experts recommend assuming that the same interactions occur with ECPs and therefore doubling the dose of ECPs (85). It is unlikely that broad-spectrum antibiotics reduce the efficacy of ECPs (456).

## Increasing Access to ECPs

More women and more providers need to know about ECPs. Also, access to ECPs should be improved both for women in general and for groups with special needs.

### Educate about ECPs

**Women.** The public—and women in particular—need to know about ECPs and how to get them. Emergency contraception should be discussed with women at routine health care visits, although at this point it seldom is (229). A study of US college students found that those who had correct information about ECPs—particularly about their ingredients and side effects—had more favorable attitudes toward their use (186, 453). The mass media can tell the public about this “new” way to avoid unwanted pregnancy, explain where to get ECPs and how to use them, stress the need to take the first dose as soon as possible and within 72 hours after intercourse, and clarify that ECPs do NOT cause abortion. Health care providers can tell women how to use their usual brand of OCs as emergency contraception, if their brand contains norgestrel or levonorgestrel. Women can be encouraged to keep an extra packet of pills on hand specifically for emergency use if needed. Where prescriptions are required for OCs and ECPs, the prescriptions can be provided ahead of time. Providers may give women an Emergency Contraception Kit consisting of instructions and pills or else a prescription that can be filled either immediately or when needed (518).

**Providers.** All women's health care providers should know about ECPs, including which pills to use, correct regimens, and possible side effects. In some places, however, many health care providers do not know that some of the same pills used for ongoing contraception can also be used for emergency contraception. Other providers may confuse ECPs with abortifacient drugs, which, in contrast to ECPs, act after implantation to disrupt an established pregnancy (9, 79, 110, 149, 157, 231, 259, 316, 326, 406, 513). In either case women may be denied information or access to ECPs because providers are not well informed. At facilities that provide ECPs, all staff members—including those who first greet clients—should know that ECPs are available.

## Make access to ECPs easy

**Make referrals simple.** Easy referrals lead to quicker treatment. Where telephones are widely accessible, hotlines can provide information about ECPs and referrals to providers. In the US and Mexico, nationwide 24-hour-a-day, toll-free hotlines provide information and referrals: 1-888-NOT-2-LATE in the US and 01-800-EN-3-DIAS in Mexico. The British Pregnancy Advisory Service maintains an “action line”—08457 304030—that offers referrals. In China hospitals have set up their own information and referral lines (32). Women in Sri Lanka can dial 501 315 on weekdays between 8:00 am and 4:30 pm for ECP information and referrals (1).

**Train a range of providers.** Pharmacists, as well as others, can provide ECPs on a woman's request. A pilot project in the US state of Washington allows pharmacists to provide ECPs according to a clear written protocol. Within the first several months the pharmacists had prescribed over 2,000 courses of ECPs, and users reported no adverse outcomes (65, 212, 226). A survey of women who had received ECPs through these pharmacists found that half obtained them on a weekend or in the evening—times when they could not usually visit a doctor's office for a prescription (212). A similar pilot project is underway in the UK, where chemists in 16 pharmacies have undergone training and are giving ECPs to women according to a specific protocol. The project will be evaluated, and a decision will be made whether to extend it (187).

**Remove unnecessary medical barriers to access.** Some providers continue to require a gynecological examination and/or pregnancy test before dispensing ECPs. These procedures are costly, use precious time, and may actually discourage some women from using ECPs (470). Likewise, the inclusion of a urine pregnancy test in commercial emergency contraception kits may deter some women from using ECPs. The test adds to the cost of the kit, requires instructions that may confuse or discourage women with limited literacy, or, if the test is negative, may falsely reassure women that their recent act of unprotected intercourse did not result in pregnancy (174).

**Offer ECPs over the counter.** Most women decide for themselves when they need emergency contraception, and a physical exam is not necessary. Therefore, well-labeled ECPs should not require a prescription and can be offered over the counter (123, 473). Over-the-counter access can make treatment more effective because women can get ECPs sooner. On June 1, 1999, the progestin-only ECP *NorLevo* was granted over-the-counter status in France. This is the first dedicated EC product to become available over the counter in a major market (52). A study conducted by the Population Council in India found strong support for over-the-counter provision of ECPs among women themselves (230). Some argue that contact with a health care provider for ECPs is an important point of entry into the health care system for some women, as well as an opportunity to discuss ongoing contraceptive needs (25). While counseling is valuable when providing any contraceptive method, access to ECPs should



not be denied because a health care provider cannot counsel the woman face to face. Women can learn about ECPs in other ways. If necessary, pharmacists can give women ECPs and refer them elsewhere, if they wish, for later counseling about ongoing contraception.

### **Serve groups with special needs**

**Youth.** There are many reasons that adolescents especially need ready access to ECPs. The psychological, social, and health risks of an unwanted pregnancy are especially great for adolescents (298, 541). At the same time, sexual activity among youth tends to be more sporadic and less likely to be planned for than among adults, and young people may be more likely to take risks. Furthermore, as US research finds, adolescents tend to wait some time between starting sexual activity and seeking reproductive health care, including contraception (6, 136). Because family, school, and society at large often disapprove of adolescent sexual activity, many young people lack adequate and appropriate information on sexuality and family planning as well as access to reproductive health care (541). Not only can emergency contraception help prevent unwanted pregnancies and abortions in this vulnerable group, but also providing ECPs sometimes can create opportunities to offer other reproductive health services and counseling about healthy sexual behavior (53, 541).

**Women suffering domestic violence.** Emergency contraception is a pressing need for many battered women (33). Women abused by their husbands or boyfriends often are unable to negotiate the timing or the terms of sexual intercourse (see *Population Reports, Ending Violence Against*

*Women*, Series L, No. 11, December 1999). A violent sexual partner may prevent a woman from using ongoing contraception, thus putting her at risk of an unintended pregnancy (292). Some women cannot discuss contraception with their partners for fear that it would spark abuse (193). An unintended pregnancy can also prompt a violent episode from an abusive partner (266). Thus access to ECPs is especially critical for battered women. ECPs should be available wherever women may seek help or refuge, such as hospital emergency rooms, counseling centers, and women's shelters (129).

**Refugees.** Refugees often are cut off from a supply of contraceptives. Furthermore, women are targets for sexual violence both while fleeing and once they arrive in refugee camps. For example, an International Rescue Committee assessment of Burundi refugees in an established camp found that 26% of women ages 12 to 49 had experienced sexual violence since becoming refugees (322). Thus emergency contraception should be available as a part of reproductive and mental health services for refugees (165). Humanitarian aid groups increasingly are making ECPs available in times of crisis (151, 476). The WHO New Emergency Health Kit (NEHK '98) and the Minimal Initial Service Package (MISP) both include written guidelines and supplies for emergency contraception (338). The High Commissioner for Refugees, the United Nations Population Fund, and WHO have produced a refugee reproductive health manual that includes guidelines for counseling and treating refugee women who are victims of sexual violence. The manual covers provision of ECPs (477).

## **For More Information**

**The Consortium for Emergency Contraception** operates an Internet website in English, French, Spanish, and Portuguese. The site offers information and advocacy materials as well as a newsletter on the status of ECPs worldwide (<http://www.path.org/cec/>). The Consortium also produces *Emergency Contraceptive Pills: A Resource Packet for Health Care Providers and Programme Managers*. This packet contains a training curriculum, sample client brochures, a medical guide, answers to common questions about EC, guidelines for introduction, and a list of selected references. Contact: Elisa Wells, Consortium Coordinator, 3224 Purdue Street, Anchorage, AK 99508, USA. By e-mail: [ewells@path.org](mailto:ewells@path.org).

**Princeton University Office of Population Research** operates a website with information on emergency contraception, a guide to US clinicians who provide emergency contraception, and country-specific information on dosages of commonly available combined and progestin-only pills for emergency use (<http://opr.princeton.edu/ec/> or <http://www.not-2-late.org>).

**MEXFAM** runs a website in Spanish and English with information on contraception, including ECPs. The site includes dosages and instructions for emergency use of pills common in Mexico (<http://www.mexfam.org.mx/>).

**Pathfinder International** publishes a comprehensive reproductive health and family planning training curriculum with a module (Module 5) that specifically addresses emergency contraception. The manual is available on the Pathfinder International website (<http://www.pathfind.org>) or by writing to Medical Services Division, Pathfinder International, 9 Galen Street, Suite 217, Watertown, MA 02172, USA.

**The Program for Appropriate Technology in Health (PATH)** and the **Northwest Emergency Contraception Coalition** produce the publication *Emergency Contraception: A Resource Manual for Providers* (<http://www.path.org/acog/>). They also provide a website that features two client brochures available in 13 languages and adaptable to suit local audiences ([http://www.path.org/resources/client\\_mtls\\_diverse\\_audiences.htm](http://www.path.org/resources/client_mtls_diverse_audiences.htm)). (See illustrations on p. 21.)

**Women's Capital Corporation** runs a website in English and Spanish about *Plan B*, the only dedicated progestin-only emergency contraceptive pill approved by the US Food and Drug Administration (<http://www.go2planb.com/>). Or contact Women's Capital Corporation, P.O. Box 5026, Bellevue, WA 98009-5026, USA; Tel: 1-800-330-1271.

**Family Health International (FHI)** publishes a teaching module entitled *Emergency Contraceptive Pills* in English, Spanish, and French. Contact: CTU Modules Project Administrator, FHI, P.O. Box 13950, Research Triangle Park, NC 21109, USA.

**The Population Council**, through its INOPAL III project, produces copies of the Consortium for Emergency Contraception's EC packet in Spanish and Portuguese. For Spanish-language materials contact: Ricardo Vernon, The Population Council Latin America and the Caribbean, Escondida no. 110, Col. Villa Coyoacán, México 04000 D.F., México; Tel: (52-5) 659-8541/8537; Fax: (52-5) 554-1226. For Portuguese-language materials contact: Loren Galvão, The Population Council Brasil, Rua Ruy Vicente de Mello, 1047 Cidade Universitária 13084-050, Campinas, São Paulo, Brasil; Tel: (55 19) 289-2495 or 249-0122. The Population Council also maintains a Spanish-language website (<http://www.en3dias.mx/>).

**Johns Hopkins Program for International Education in Reproductive Health (JHPIEGO)** produces the website *Reproductive Health Online (ReproLine)* (<http://www.reproline.jhu.edu>). The site has a section on ECPs, including presentation graphics and supporting documentation.



(Text continues from page 16.)

women per year can be attributed to VTE. Based on recent case-control studies, an estimated 1.3 to 2.4 additional deaths per million women per year occur among OC users (131).

**Increased blood pressure and hypertension.** Many studies have found small but statistically significant increases in blood pressure in women taking combined OCs with 50 µg of estrogen or more (42, 137, 138, 300, 435, 510, 511, 525). Increases averaged about 6 mm Hg for systolic blood pressure and 2 mm Hg for diastolic blood pressure (417). Studies have reported generally comparable increases in blood pressure among users of low-dose combined OCs as well (162, 241, 320, 327, 525, 534).

In some women these increases are enough to lead to a diagnosis of hypertension (blood pressure of 140/90 or higher). Usually, however, blood pressure remains within normal ranges and declines once the woman stops using OCs (55, 71, 137, 241, 510). For example, a recent US cohort study of about 68,000 nurses ages 25 to 42 found that, after adjusting for other possible risk factors, OC users were almost twice as likely to develop hypertension as women who had never used OCs. Risk increased with duration of use but decreased rapidly after women stopped using OCs (71).

### Other Health Risks

OCs have been associated with changes in carbohydrate metabolism and with increased risk of gallbladder disease and noncancerous liver tumors.

**Carbohydrate metabolism and diabetes.** Combined oral contraceptives may affect carbohydrate metabolism in two ways. The estrogen component is thought to increase glucose levels and suppress the insulin response to them. The higher the dose, the more effect (153, 156, 544). The progestin component has been hypothesized to stimulate overproduction of insulin, a suspected risk factor for atherosclerosis (96, 544, 545).

In low-dose OC users with initially normal blood sugar levels, these responses seldom exceed the normal range. These women face no apparent risk of developing diabetes (143, 152, 158, 171, 185, 385).

Can women with diabetes use combined OCs? Diabetics, whose insulin response to increases in glucose is already suppressed, may still be able to use low-dose OCs, depending on the severity of their diabetes. If they are insulin-dependent, their insulin requirement may increase, although with low-dose pills this does not appear to happen often (48, 305). Diabetics with known vascular disease or women who have had diabetes for over 20 years (and therefore may have suffered vascular damage) generally should choose another family planning method (557). Women with a history of diabetes during pregnancy or a family history of diabetes can safely use combined OCs without special medical supervision (48, 177, 189, 190, 228, 280, 538).

**Gallbladder disease.** OCs probably do not cause gallbladder disease, but instead they may accelerate the development of gallstones in already susceptible women. Gallstones are caused by abnormally high saturation of bile with cholesterol. Cholesterol saturation is higher in OC users than nonusers, possibly due to estrogen (432, 526).

After finding a higher risk during the early years of OC use, the major cohort studies did not detect any elevated risk of gallbladder disease among long-term OC users. The lack of long-term risk suggests an acceleration effect in women with already high cholesterol saturation (318, 375, 494, 526). An analysis of the results of several studies from the 1970s and early 1980s concluded that OC use is associated with only a slight increase in the risk of gallbladder disease (458).

There may be little or no increased risk with low-dose formulations (458, 494). More recent analyses have found either no increased risk of gallbladder disease or, at most, a small, transitory increased risk among current OC users. An analysis of 25 epidemiologic studies concluded that only nine studies used rigorous methodology. These nine studies detected a 30% to 40% increased risk of gallbladder disease in OC users, although the increases were not statistically significant. Since 1982 no studies have reported relative risks as high as 1.5 (458).

Because of concerns that OCs may worsen existing gallbladder disease, WHO recommends that women with current symptoms of the disease should choose another method if possible (538).

**Noncancerous liver tumors.** Noncancerous liver tumors (hepatocellular adenomas), which are rare, are somewhat more frequent in OC users than in nonusers. They can be fatal if untreated (483). Their incidence increases with higher estrogen dose and longer OC use. Studies in the 1970s of women using higher-dose pills estimated that three cases attributable to OCs would occur per 100,000 users per year. With today's low-dose OCs, this rate may be lower (277), but new studies have not been conducted. (See p. 31 for discussion of liver cancer and OCs.)



*In Thailand a community-based distributor who travels by boat gives a client a packet of pills. Oral contraceptives are well suited to community-based distribution and social marketing because of their safety and because using them involves no medical procedure.*



## Drug Interactions

Contraceptive hormones can interact with certain other drugs, reducing the effectiveness of OCs or modifying the effects of the other drugs. Pregnancies and breakthrough bleeding due to interference with contraceptive hormones have been reported in OC users taking:

- The anticonvulsant drugs carbamazepine, ethosuximide, methylphenobarbital, paramethadione, phenobarbital, phenytoin, primadone, and topirimate;
- The antitubercular antibiotic rifampicin; and
- The antifungal drug griseofulvin.

Although anecdotal reports have suggested that broad-spectrum antibiotics such as ampicillin and tetracycline might also interfere with OC effectiveness, research has not demonstrated this (18, 19, 23, 333, 377, 418-422, 450, 508).

If a user of low-dose OCs is taking any of these drugs, she can increase her contraceptive protection by using an additional method of contraception while continuing with her daily pill, or she can change to an OC with 50 µg estrogen. If she uses the drug for less than a month, she should continue using her back-up contraceptive method or different pill regimen for at least a week after stopping the drug. If her cycle of 21 contraceptive pills ends during this week, for best protection she can start the next cycle of pills immedi-

ately. If she is using 28-day pill cycles, she can skip the seven placebo or iron tablets and start the next cycle of pills immediately (178, 189).

Women who must take any of these drugs for a long time, such as women being treated for tuberculosis, may want to consider another contraceptive method. Alternatively, they may increase their contraceptive protection by taking OCs with 50 µg estrogen for extended periods without interruption (179).

Oral contraceptives can speed up the metabolism of certain other drugs. Increased clinical effects have been observed in OC users taking anti-anxiety benzodiazepine drugs, corticosteroids used against inflammations, and theophylline (a drug used for asthma and some circulatory conditions). Thus OC users may require lower doses of these drugs than other women (18, 189, 418). Low-estrogen OCs generally speed metabolism less than high-dose pills.

## Unresolved Health Issues

OCs have proved safe for most women. Still, several important health issues remain unresolved, even though the perspective of these issues has become clearer. Of particular concern are associations between OC use and neoplasia of the cervix and breast. Women who use OCs may have slightly elevated risks of being diagnosed with cervical neoplasia and early occurring breast cancer—risks which disappear within 10 years after discontinuing use. In both cases screening bias cannot be ruled out as an explanation for the apparent risk. The OC users studied tend to have more regular gynecological care than other women, and thus early cancer may be more likely to be detected in these women. OC use has been linked to an increased risk of certain reproductive tract infections, including HIV. While an association is biologically plausible, possible methodological problems make interpretation difficult. Finally, results of recent studies conflict as to whether OCs are linked to hepatocellular carcinoma, a rare form of liver cancer.

### Cervical Cancer

Certain strains of human papillomavirus (HPV) are widely considered to be the primary initiator of cervical cancer. Epidemiologic evidence remains inconclusive on whether OCs play some secondary role in the development of cervical cancer. Most early studies found no link between OC use and malignant or premalignant cervical neoplasms. In general, the earlier studies did not include long-term OC users (491). Recent studies have been fairly consistent in finding somewhat greater risk of cervical cancer or its precursors among users of combined OCs than among other women (112). Whether this reflects a cause-and-effect relationship is not clear, however.

**Epidemiologic findings on preinvasive lesions.** Most studies in the past 10 years have found an association between OC use and cervical intraepithelial neoplasia (CIN) and carcinoma in situ (CIS), collectively described as pre-invasive lesions. Pre-invasive lesions fall into two general categories: LSIL (low-grade squamous intraepithelial lesions), which correspond to mild dysplasia (abnormal tissue development), and HSIL (high-grade squamous intraepithelial lesions), which correspond to moderate and severe dysplasia and CIS (44).

## Have your Cervix Screened for Cancer today!



**For more information visit our clinics at ...**

Where treatment is available, cervical cancer screening can benefit all women. This Kenyan poster invites women for cervical screening.



# Preventing Cervical Cancer

Cervical infection with some types of human papilloma-virus (HPV) appears to cause most, if not all, cases of cervical cancer (126, 372). A recent analysis of 1,000 cervical cancer specimens collected worldwide found evidence of HPV infection in 99.7% of the samples (502). Many women develop HPV infections, but few go on to develop cervical neoplasia. HPV infection usually is transient and clears without treatment (199). Apparently, cancer arises from infections that persist—perhaps those lasting six months or more (203, 383).

## Avoiding HPV

Primary prevention of cervical cancer is the ideal, and that means minimizing exposure to HPV. A woman can reduce her exposure to HPV and other sexually transmitted disease organisms by using a barrier method of contraception—preferably condoms, but perhaps also diaphragms and spermicides—whether or not she also uses another family planning method such as OCs. Abstinence and delaying first sexual intercourse also reduce the risk (173). The behavior of women's sexual partners is important. Men who were young when they first had sexual intercourse, who have multiple sexual partners, or who visit prostitutes regularly increase their partners' risk of cervical cancer significantly (107, 317, 462).

It may be particularly difficult for a sexually active woman to avoid HPV. Identifying an uninfected sexual partner—and knowing one's own status—is not possible without testing. Moreover, the types of HPV that cause cervical cancer do not cause warts (235) or any other obvious symptom. At the same time, the virus is very common. Condoms are helpful, but HPV can spread through contact between areas of the body near the anus or genitals that a condom does not cover (423). HPV vaccines are being developed, but the availability of a safe and effective vaccine is probably over a decade away (215, 372).

Relative risks of pre-invasive lesions were for the most part less than 2.0—for example, 1.3 for ever-use (546), 1.4 for past users (169), and 1.8 for low-grade lesions (323). A Swedish study found current use of OCs to be associated with a fourfold increase in risk of pre-invasive lesions overall; risk increased with duration of use (547). One recent study, however, found no association between OC use and pre-invasive lesions (80). For women who had used OCs for five years or more, several recent studies report about a doubling of risk compared with women not using the pill (46, 47, 245, 546). Studies that have looked at various grades of pre-invasive lesions, however, have reported inconsistent findings (46, 251, 323).

**Epidemiologic findings on invasive cancer.** As with pre-invasive lesions, most studies in the past decade have found that long-term OC use is associated with a slight increase in risk of invasive cervical cancer (304). In many of these studies risk increased with duration of use (43). An analysis of 14 studies found relative risks of invasive cervical cancer to be 1.37, 1.60, and 1.77 for 4, 8, and 12 years of OC use (410).

While HPV infection may initiate most or all cervical cancers, cigarette smoking poses an increased risk (523, 527), and avoiding smoking will limit risk. A diet rich in vitamin C may also help (173).

## Screening

Since most women cannot eliminate all chances of exposure to HPV, where feasible, women should be screened for cervical lesions. The Papanicolaou (Pap) smear is the current standard screening method. Pap smears can identify cervical neoplasia at early stages, when treatment is almost always effective. Countries that have instituted national screening programs have seen deaths from cervical cancer decline to one-third or less of previous levels (384). Unfortunately, comprehensive Pap screening is practically nonexistent in developing countries, where cervical cancer is the most common type of cancer among women.

A more feasible screening technique appears to be on the horizon. Visual inspection of the cervix after an acetic acid (vinegar) wash—also known as cervicospoty, or VIA—offers a low-cost, low-tech alternative to the Pap smear. Lesions appear white after application of vinegar and can be seen with a flashlight (220). In Zimbabwe nurse-midwives using this method accurately detected more than 75% of pre-invasive lesions compared with 44% with Pap smears (479). Similarly, in India paramedical personnel could accurately detect pre-invasive and invasive lesions using VIA (402). In India, VIA was as specific—able to detect accurately women who do not have pre-invasive or invasive lesions—as a Pap smear (402), while in Zimbabwe VIA was less specific than a Pap smear (479). Early detection allows for early treatment with low-cost, easy methods such as cryotherapy—freezing the cervix with a liquid coolant to destroy abnormal tissue—that nurse-midwives and many other health care providers can administer (220).

Some evidence suggests that OCs accelerate the progression of precancerous lesions to invasive cancers. Any increased risk may be concentrated in current and recent users (26, 344). One study found that no increased risk persisted beyond 10 years after OC use ended (344). Another study found that OCs increased the risk of invasive cancer only when first used at a young age, especially at age 17 or younger, a crucial time in the development of a woman's reproductive tract (101).

**Interpreting the findings.** A number of biological mechanisms have been proposed to explain an association between OCs and cervical neoplasia. Currently, no firm evidence favors any one of these mechanisms. It has been suggested that OCs might: (1) promote the growth of existing lesions, (2) change cervical mucus to increase tissue susceptibility to HPV (491), (3) alter immune response to increase susceptibility to HPV, (4) produce a folate deficiency in the cervix that could stimulate development of abnormal lesions (144, 408), and/or (5) enhance genetic replication of HPV (43, 161, 183, 216, 350, 426).





This primary health center in Nepal displays a wall painting near the entrance that promotes oral contraceptives. In many clinics worldwide, health care providers help clients choose the contraceptive method that best suits their individual needs.

Observed associations between cervical neoplasia and OCs may reflect the difficulties of studying the issue rather than causal relationships. First, OC use may be part of larger behavior patterns that also increase the risk of cervical cancer (430). Second, cervical neoplasia may be more easily detected in OC users than in other women (detection bias). These difficulties are hard to overcome completely. Furthermore, the biological factors that influence the development of cervical cancer are complex.

**Behavioral factors.** Studies of cervical cancer and OCs may need to take account of both sexual behavior and smoking. Sexual behavior, particularly age of first intercourse, lifetime number of sexual partners, and use of barrier contraception, are known to affect the risk of developing cervical cancer. Younger age at first intercourse and more partners raise risks. Condom use lowers risks. If women choose OCs because they start sexual activity early or have many sex partners, and they do not use condoms, studies would find a noncausal association between OC use and cervical cancer (64).

There is fairly strong evidence associating cervical cancer and cigarette smoking (523, 527). Several studies suggest about a twofold increase in risk for smokers compared with nonsmokers (46, 102, 168, 547). A Danish study suggested that OC users who smoke are at particularly high risk of cervical cancer. Among women using OCs for six years or more, smokers had a relative risk of 6.0 compared with 2.2 among nonsmokers (245).

**Detection bias.** In developed countries OC users tend to have more Papanicolaou (Pap) smears than other women do to test for cervical cancer and its precursors (64). Therefore, asymptomatic cervical neoplasia may be detected earlier among OC users, and false positive diagnoses may be more common. Changes in the cervix induced by OCs may make

pre-invasive lesions easier to detect, or they might make OC users more susceptible to vaginal infections that can be mistaken for pre-invasive lesions (169, 183). In either case the result would be *detection* of more lesions in OC users, but not actually more lesions.

**Biological factors.** Cervical cancer develops slowly. Invasive cancer apparently occurs at the end of a slow progression of pre-invasive lesions. But most mild, and many moderate, pre-invasive lesions regress spontaneously (93, 206). Very few progress to invasive cancer (321, 383). Risk factors for progression at each stage—and for progression to invasive cancer—may vary (44). Hypothetically, OC use could have an independent effect or act as a cofactor at any stage. Thus a causal link between OC use and pre-invasive lesions—if established—would not necessarily imply a link to invasive cancer (184, 346). Research needs to explore why some pre-invasive lesions progress while most regress, and what role, if any, OCs play in progression.

Because HPV is the primary cause of cervical cancer (see box, p. 27), researchers have looked for a connection

between OCs and the risk of acquiring HPV infection. Findings are mixed. Some studies have reported that OC users are significantly more likely to acquire or have an HPV infection (159, 271, 283, 323, 395, 459, 487). Others have not (24, 51, 198, 233, 279, 367, 426, 449, 489). Studies have not consistently controlled for sexual behavior, however.

HPV targets cervical cells that are actively dividing (244). OCs increase cervical ectopy—the extension of sensitive columnar epithelial cells from the cervical canal to the vaginal surface of the cervix. Thus it is possible that OCs could enhance susceptibility of the cervix to HPV infection (216).

## Breast Cancer

The possible role of OCs in the development of breast cancer has been debated for over three decades. Some breast cancers are hormone-dependent, and breast cancer is an increasingly common cause of death among older women, particularly in developed countries. Thus many studies have sought to find out if OC use affects the risk of developing breast cancer (521). In 1996 the Collaborative Group on Hormonal Factors in Breast Cancer published an analysis that pooled epidemiologic evidence from 54 studies in 25 countries (82, 83). Covering over 53,000 women with breast cancer and over 100,000 without breast cancer, these 54 studies constituted about 90% of the epidemiologic evidence available at the time. The analysis examined a great many characteristics of OC use and users.

Findings from the pooled analysis include:

- Overall, women currently taking OCs or who have quit use within the past 10 years were slightly more likely than nonusers to be *diagnosed* with breast cancer.



- Risk was greatest for current users and decreased with time between last use and diagnosis. Relative risk was 1.24 for current users, 1.16 for women who had stopped use within one to four years before diagnosis, and 1.07 for women who had stopped use five to nine years before diagnosis.
- There was no additional risk for OC users who discontinued use 10 to 20 years before diagnosis. In some subgroups former OC users faced less risk than nonusers.
- The excess risk of breast cancer diagnoses in OC users was solely for cancers that were localized. OC users actually had a reduced risk of cancers that had spread beyond the breast.
- Women who used OCs before age 20 faced somewhat higher relative risk, when compared with nonusers of the same age, than women who used OCs later in life.
- Whether a woman first used OCs before or after she first gave birth did not appear to make much difference.
- For women with a family history of breast cancer, OC use did not seem to increase risk particularly.
- Duration of OC use did not affect risk.
- Data were limited, but risk did not appear to be related to type of estrogen or progestin, and the only dose-related difference was a reduction in breast cancer among women who had used the highest dose pills more than 10 years before (82, 83).

This pattern of findings suggests two possible explanations of a relationship between OC use and breast cancer. First, OCs may promote the growth of an already existing tumor. The observations that relative risk is greatest during and soon after OC use and that duration of OC use has no effect on risk argue that OCs do not initiate new tumors. Second, OC users may simply have more frequent and more careful breast exams than other women, and thus their tumors may be found at an earlier stage. The fact that the entire excess risk of breast cancer diagnosis occurs for tumors that are localized and that OC users actually have a reduced risk of cancers that are spread beyond the breast strongly supports this possibility. The Collaborative Group researchers comment:

*The relation observed between breast cancer risk and hormone exposure is unusual, and it is not possible to infer from these data whether it is due to an earlier diagnosis of breast cancer in ever-users, the biological effects of hormonal contraceptives, or a combination of reasons. (82)*

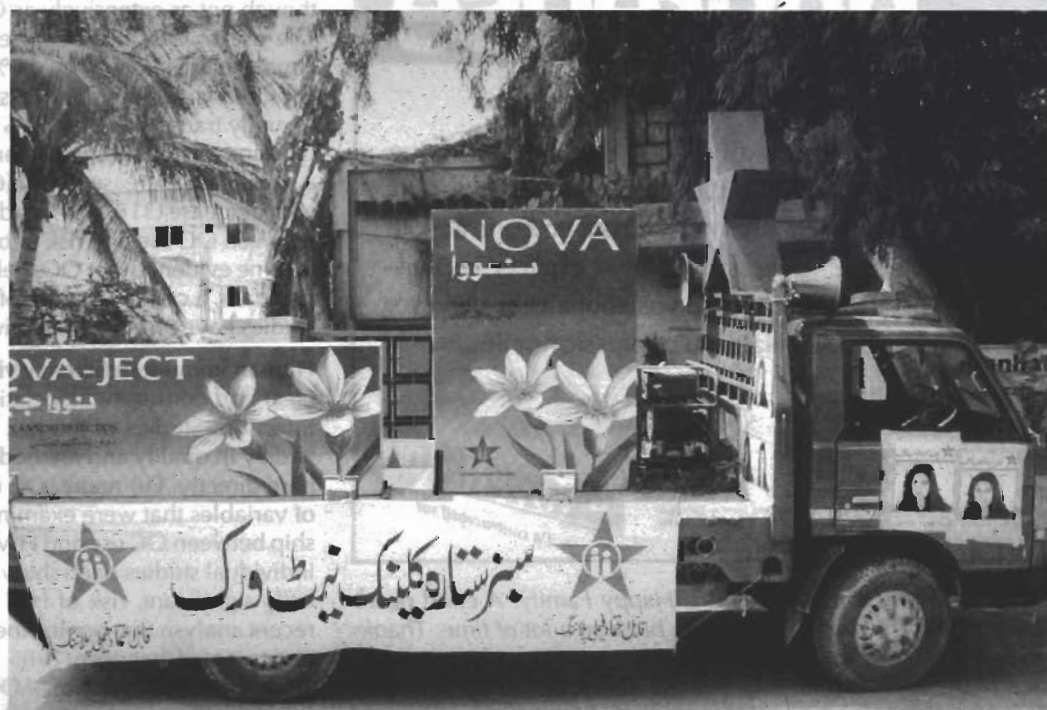
The finding that the modest additional risk is greatest during OC use and eventually disappears after a woman stops OCs has important public health implications (521). Because most women use OCs when they are young, and breast cancer is extremely rare at

young ages, the number of breast cancer cases attributable to OC use would be quite small. By the Collaborative Group's estimate, among 10,000 European or North American women using OCs from ages 16 to 19, an additional 0.5 cases of breast cancer would be diagnosed in the 10 years after these women quit OC use; among those using OCs from ages 20 to 24, 1.5 additional cases; and among those using OCs from ages 25 to 29, 4.7 additional cases. Because of this age gradient, earlier OC use in a population does not lead to more cancers diagnosed overall (82). Generally, the numbers of additional cases would be smaller in developing countries, where breast cancer is less common (83). By 20 years after stopping OC use, there was no significant difference between women who used OCs at these ages and nonusers in the cumulative number of breast cancer cases diagnosed.

Since the Collaborative Group's analysis in 1996, OCs and breast cancer continue to be studied. A US study involving 744 breast cancer patients found effects largely compatible with the findings of the Collaborative Group, but for the most part increased risks were not statistically significant (480). A small case-control study in Nigeria found that women diagnosed with breast cancer were more likely to have used OCs. The analysis did not control for other risk factors such as age at first birth, however, and information about duration of use and pill formulation could not be obtained (5). Like the Collaborative Group analysis, the German Breast Cancer Study Group found that the breast tumors of OC users tended to be smaller at diagnosis. OC use did not significantly affect the length of recurrence-free survival or of overall survival, however (405).

## Reproductive Tract Infections

The relationships between OC use and reproductive tract infections (RTIs), which include both those that are sexually transmitted and those that are not, are varied and complex.



A parade float promotes social-marketed Nova brand oral contraceptives and injectables in Pakistan.



Therefore it is difficult to determine whether pill use affects chances of developing an RTI. For example, if women who use the pill tend to have more sexual partners and more frequent intercourse and are less likely than other women to use condoms, these behavioral differences themselves expose women to greater chances of acquiring a sexually transmitted infection (STI). For protection against STIs—including HIV, the virus that causes AIDS—latex condoms are the best method and can be used along with OCs (see **Population Reports**, *Closing the Condom Gap*, Series H, No. 9, April 1999).

**Chlamydial infection.** Most recent studies find an association between use of OCs and infection with *Chlamydia trachomatis*, the most common STI (2, 4, 17, 35, 37, 97, 244, 284, 285, 331, 553). Older studies found a two- to threefold increase in risk of chlamydia among OC users (506). Some recent studies have found less increase, about 70% more than nonusers, and others have found no increase in risk (347, 374, 394, 509).

Greater risk of chlamydial infection among pill users could be due largely to cervical ectopy. Cervical ectopy is the extension of sensitive columnar epithelial cells from the cervical canal to the vaginal surface of the cervix. It is known to occur in OC users (219). Cervical ectopy may make columnar cells easier targets for *C. trachomatis* (17, 30, 94, 392). Several studies confirm a link between ectopy and chlamydial infection (284, 347, 374). These studies, however, could not determine which came first—ectopy or infection—and so it is not clear whether ectopy leads to infection or infection leads to ectopy. Similarly, in studies of chlamydial infection and OCs, it is possible that ectopy simply makes it easier to detect the infection (17, 505).

**Chlamydial pelvic inflammatory disease (PID).** For more than 10 years there has been considerable speculation about whether or not OCs actually offer some protection against PID caused by the ascent of chlamydial infection from the cervix into the fallopian tubes. Although OC users seem more susceptible to chlamydial infection than other women do, they are less likely to experience symptomatic chlamydial PID. For example, two recent studies found that pill users faced 20% to 30% as much risk of chlamydial PID as women using nonhormonal methods (242, 439).

How would OCs help protect against chlamydial PID? Possible explanations include reduced penetrability of cervical mucus, reduced uterine contractions during menses, and alteration of immunological response (36). Whether any of these mechanisms apply, however, is not certain.

Furthermore, most studies of PID have involved only women hospitalized for PID, which accounts for less than one-quarter of cases (439). Women hospitalized for PID are not representative of all women who have PID. Chlamydial PID, moreover, is less likely to lead to hospitalization than other forms of PID because chlamydial PID tends to be milder and less often noticed (340).

**Other reproductive tract infections.** Possible associations between OCs and other RTIs have also been studied, although not as extensively as OCs and chlamydial infection. The use of OCs has been reported to increase the risk of gonorrheal infection by 70% (284, 392) and the risk of candidiasis, a common yeast infection that is not usually sexually transmitted, by 50% to 80% (67, 392). Findings on OCs and bacterial vaginosis are conflicting. One study found a significant increase in risk (67); some have found a significant decrease (310, 424); and another found no relationship between OC use and risk of bacterial vaginosis (176). There is some evidence that OCs help protect against *Trichomonas vaginalis*, a common cause of vaginitis (22), although not all studies have found a protective effect (331).

**Human immunodeficiency virus (HIV).** Studies fail to show clear and consistent associations between OC use and HIV infection. Studies of the risk factors for HIV infection vary widely in quality and methodology and are difficult to compare directly. For many, OC use was only one of a number of variables that were examined, and the potential relationship between OC use and HIV was not the focus of the study. Individual studies often show elevated, although not statistically significant, risk of HIV infection among OC users. A recent analysis that pooled the results of 28 studies published or presented between 1985 and 1999 found a significant association between use of OCs and the incidence or prevalence of HIV infection. Based on the eight studies considered methodologically most sound, OC use was associated with

**Famille**

**heureuse**

Un enfant a besoin qu'on lui donne beaucoup d'amour mais aussi qu'on lui consacre beaucoup de temps. Grâce à **Novelle Duo**, un contraceptif fiable et efficace, vous pouvez espacer les naissances en fonction de vos souhaits et de votre situation familiale ou professionnelle.

400 PCFA la boîte de 2 plaquettes

**Novelle Duo**  
Un contraceptif sûr

Novelle Duo est distribué par FM.S.C. (Programme de Marketing Social au Cameroun)  
BP 14025 Yaoundé - Tél./fax: 23 92 24 - BP 4889 Douala - Tél./fax: 43 29 28 - Expertise PSI

This poster from Cameroon states: "Happy Family: A child needs someone who gives him a lot of love but also a lot of time. Thanks to Novelle Duo, a reliable and effective contraceptive, you can space births according to your wishes and your family or professional situation." For many women, both high effectiveness and convenience are important reasons for choosing oral contraceptives.



a 60% increase in risk (504). Studies of OCs and HIV may not be suitable for a pooled analysis, however. One recent review of the literature on the association between OCs and HIV infection concludes that studies to date suffer from methodological limitations that make them inappropriate for combined statistical analysis (445).

Most individual studies have not found a statistically significant association between OC use and HIV infection (8, 63, 115, 128, 314, 330, 403, 429). A study that examined the chances of infection per sexual contact found that HIV infection was *less* likely, although not significantly so, among OC users than among women who were not OC users and were not using a barrier method (319).

Several recent studies have found a significant association between OCs and HIV among various subgroups after adjusting for a variety of confounding factors. A prospective study of 435 HIV-negative Kenyan sex workers found that over a one-year period OC users were 2.6 times more likely to become HIV positive than women not using OCs (291). Another found a link only among poor women, after taking account of condom use, number of partners, and husband having multiple sexual contacts (202). In contrast, a study of women attending a Nairobi antenatal clinic—a group considered at low risk of HIV infection—found that OC users were 3.5 times more likely to be infected with HIV than women using other methods of contraception or no contraception at all. The association persisted after adjustment for variables such as frequency of intercourse, number of partners, and history of STI symptoms. Few of these women used condoms (428).

A cross-sectional study in Nairobi suggests that OC use increases the risk of HIV infection *only* among women with genital ulcers. OC use alone did not increase HIV risk. Women who had used OCs longer than 12 months and had genital ulcer disease, however, were 25 times more likely to be infected with HIV than women who did not use OCs and did not have genital ulcers. This finding was based on 16 women who were long-term OC users and had genital ulcer disease, 80% of whom were infected with HIV (362).

Some evidence has led to speculation that HIV-infected OC users could infect their partners more readily than other HIV-infected women. In Kenyan women HIV DNA was found more often in the cervical and vaginal secretions of HIV-infected OC users than in other HIV-infected women. The higher the OC dose, the more likely that HIV DNA was present (315). Another study found that HIV-infected OC users shed significantly more HIV DNA in cervical cells than did other HIV-infected women (77). Not all studies have found a link between OCs and HIV DNA levels, however (249).

The presence of another STI increases the risk of HIV infection by two- to sixfold (56, 91, 108, 114, 205, 232, 238, 256, 303, 339, 363). Bacterial vaginosis, which is often but not always sexually transmitted (201), also has been linked to increased HIV risk (414, 451, 507). If other STIs make women more susceptible to HIV infection, and OCs make women more susceptible to other STIs, then OCs might indirectly increase HIV risk (66, 217).

Studies of OCs and HIV are particularly difficult to carry out and to interpret. As in all studies of family planning methods, ethics prevent randomly assigning women to use various contraceptive methods. Differences in sexual behavior associated with choice of methods then make it difficult to

# "The Pill is not enough!"



**"You need a condom to keep AIDS and STDs away."**

You think you know your boyfriend well.  
You think you could never get a disease from him.  
Think again.  
He may not even know he's infected.  
Use a latex condom every time.

**A condom is for both of you.**



*For protection against sexually transmitted diseases (STDs), including HIV, the virus that causes AIDS, latex condoms are the best method and can be used along with OCs. This Canadian poster urges pill users to use condoms to prevent AIDS and STDs.*

compare users of different methods. Furthermore, all study participants at risk for STIs must be encouraged to use condoms and instructed in their use, making it difficult to study the effects of OCs among women who do not use condoms. Also, uncertainty about when a woman became infected with HIV can make it hard to know if a woman was using OCs at the time of infection. Finally, differences in classifications of OC use patterns make comparisons among studies difficult.

## Liver Cancer

A number of case-control studies in developed countries have detected increased risks of a rare liver cancer, hepatocellular carcinoma, in OC users (139, 196, 254, 324, 342, 455, 548). These studies reported risks among OC users about 2 to 20 times greater than risks among nonusers. The largest of these studies found that women using OCs for eight years or more were four times more likely to develop this liver cancer than nonusers (324). In contrast, a recent study in six European countries (191) and a study of South African women (240) found no increased risk of hepatocellular carcinoma among short-term or long-term users.



More research is needed in developing countries. Hepatitis B and C, which are the most important risk factors for liver cancer, are much more common in developing countries than elsewhere (191). It is not known whether or not OCs might interact with hepatitis infection to further increase the risk of liver cancer. A WHO study in eight developing countries where hepatitis infection is widespread found no increase in risk of liver cancer associated with short-term OC use. Few women in the WHO study had used OCs for more than three years (444).

Liver cancer is quite rare, but it is usually fatal within a year of diagnosis. Therefore, if OCs significantly increased the risk of liver cancer, both incidence of the disease and mortality from it should have risen noticeably since the 1960s, when OCs were introduced. A recent study, however, found no evidence of increased incidence or mortality either in the US or in Sweden, two countries where OCs have been used

extensively since the 1960s. Instead, the study found a gradual increase in incidence of liver cancer and resulting mortality in Japan, where OCs are seldom used (501).

Despite some lingering uncertainties, the benefits of oral contraceptives far outweigh the risks for the vast majority of women. Continuing research has made it possible to identify more clearly the few women who face substantial risks and should choose another method of contraception. Forty years after their introduction, OCs remain popular for their convenience, effectiveness, and safety.

Photos and posters in this report were selected from the Johns Hopkins Media/Materials Clearinghouse collection and Photoshare database. For further information, contact the M/MC at [mmc@jhuccp.org](mailto:mmc@jhuccp.org)

**YOUR GATEWAY TO RELEVANT, RELIABLE REPRODUCTIVE HEALTH INFORMATION**

## REPRODUCTIVE HEALTH GATEWAY

[www.rhgateway.org](http://www.rhgateway.org)

### Reproductive Health Gateway—A Better Way to Find Reproductive Health Information on the World Wide Web

Tired of Searching Through Irrelevant Material? Can't Find Accurate, Reliable Information? Need Direct Access to the Best Reproductive Health Sites?



**Visit Reproductive Health Gateway**  
at <http://www.rhgateway.org>

- Easy-to-use search function currently searches through more than 36,000 pages.
- Nearly three dozen websites participating, selected for their value to reproductive health professionals.
- Search results are directly linked to the specific pages containing your search terms.

Reproductive Health Gateway is a project of the Population and Health Materials Working Group (<http://www.med.jhu.edu/ccp/>). Participants in the Working Group work with the Population, Health and Nutrition Center of the US Agency for International Development (USAID). The Johns Hopkins Population Information Program manages Reproductive Health Gateway.



# Bibliography

An asterisk (\*) denotes an item that was particularly useful in the preparation of this issue of **Population Reports**.

1. ABEYVICREMA, D. (Family Planning Association of Sri Lanka) [Hotline on emergency contraception] Personal communication, Feb. 6, 2000.
2. ACOSTA-CÁZARES, B., RUIZ-MAYA, L., and DE LA PENA, J.E. Prevalence and risk factors for *Chlamydia trachomatis* infection in low-income rural and suburban populations of Mexico. *Sexually Transmitted Diseases* 23(4): 283-288, Jul./Aug. 1996.
3. ADAM, S.A., THOROCOOD, M., and MANN, J.I. Oral contraception and myocardial infarction revisited: The effects of new preparations and prescribing patterns. *British Journal of Obstetrics and Gynaecology* 88(8): 838-845, Aug. 1981.
4. ADDISS, D.G., VAUGHN, M.L., GOLUBJATNIKOV, R., PFISTER, J., KURTZYCZ, D.F., and DAVIS, J.P. *Chlamydia trachomatis* infection in women attending urban midwestern family planning and community health clinic: Risk factors, selective screening, and evaluation of non-culture techniques. *Sexually Transmitted Diseases* 17(3): 138-146, Jul./Sep. 1990.
5. ADEBAMOWO, C.A. and ADEKUNLE, O.O. Case-controlled study of the epidemiological risk factors for breast cancer in Nigeria. *British Journal of Surgery* 86(5): 665-668, May 1999.
6. ALAN GUTTMACHER INSTITUTE (AGI). Sex and America's teenagers. New York, AGI, 1994, 88p.
7. ALLEN, H.H. Clinical assessment of a low-dose oestrogen, low-dose progestogen combined oral contraceptive. *Current Medical Research and Opinion* 2(2): 101-108, 1974.
8. ALLEN, S., LINDAN, C., SERUFLIRA, A., VAN DE PERRE, P., RUNDLE, A.C., NSENGUMUREMYI, F., CARAEL, M., SCHWALBE, J., and HULLEY, S. Human Immunodeficiency Virus infection in urban Rwanda. Demographic and behavioral correlates in a representative sample of childbearing women. *Journal of the American Medical Association* 266(12): 1657-1663, Sep. 25, 1991.
9. AMERICAN COLLEGE OF OBSTETRICIANS AND GYNCOLOGISTS. Pharmacists limit women's access to emergency contraception (Press release). [Website]. <[http://www.acog.org/from\\_home/publications/press\\_releases/Nr0599ec.htm](http://www.acog.org/from_home/publications/press_releases/Nr0599ec.htm)>. May 18, 1999. Accessed Mar. 7, 2000.
10. ANANJEVIC-PANDEY, J. and VLAJINAC, H. Myocardial infarction in young women with reference to oral contraceptive use. *International Journal of Epidemiology* 18(3): 585-588, Sep. 1989.
11. ANDERSCH, B. The effect of various oral contraceptive combinations on premenstrual symptoms. *International Journal of Gynaecology and Obstetrics* 20(6): 463-469, Dec. 1982.
12. ANNEGERS, J.R., STROM, H., DECKER, D.G., DOCKERTY, M.B., and O'FALLON, W.M. Ovarian cancer: incidence and case control study. *Cancer* 43(2): 723-729, Feb. 1979.
13. APELO, R. and VELOSO, I. Clinical experience with ethinyl estradiol and d-norgestrel as an oral contraceptive. *Fertility and Sterility* 26(3): 283-288, Mar. 1975.
14. APELO, R.A. and SUPLIDO, A. Clinical assessment of a new triphasic oral contraceptive. *Clinical Therapeutics* 8(1): 61-70, 1985.
15. ARMSTRONG, J.L., REID, M., and BIGRIG, A. Scare over oral contraceptives. Effect on behaviour of women attending a family planning clinic [letter]. *British Medical Journal* 311(7020): 1637, Dec. 16, 1995.
16. ARNT, I.C., FERRARI, A., SARTORETTO, J.N., and WOUTERSZ, T.B. Low-dose combination oral contraceptives: A controlled clinical study of three different norgestrel-ethinyl estradiol ratios. *Fertility and Sterility* 28(5): 549-553, May 1977.
17. AVONITS, D., SERCU, M., HEYERICK, P., VANDERMEEREN, I., MEHEUS, A., and PIOT, P. Incidence of uncomplicated genital infections in women using oral contraception or an intrauterine device: A prospective study. *Sexually Transmitted Diseases* 17(1): 23-29, Jan./Mar. 1990.
18. BACIEWICZ, A.M. Oral contraceptive drug interactions. *Therapeutic Drug Monitoring* 7(1): 26-35, Mar. 1985.
19. BACK, D.J. and ORME, M.L. Pharmacokinetic drug interactions with oral contraceptives. *Clinical Pharmacokinetics* 18(6): 472-484, Jun. 1990.
20. BACKSTROM, T., HANSSON-MALMSTROM, Y., LINDHE, B.A., CAVALLI-BORKMAN, B., and NORDENSTROM, S. Oral contraceptives in premenstrual syndrome: A randomized comparison of triphasic and monophasic preparations. *Contraception* 46(3): 253-268, Sep. 1992.
21. BADRAOUI, M.H. and ASKALANI, H. Effect of low-dose combined OCs on lactation patterns. *Contraceptive Delivery Systems* 4(4): 327-329, Sep. 1983.
22. BARBONE, F., AUSTIN, H., LOUV, W.C., and ALEXANDER, W.J. A follow-up study of methods of contraception, sexual activity, and rates of trichomoniasis, candidiasis, and bacterial vaginosis. *American Journal of Obstetrics and Gynecology* 163(2): 510-514, Aug. 1990.
23. BARNETT, M.L. Inhibition of oral contraceptive effectiveness by concurrent antibiotic administration. A review. *Journal of Perinatology* 56(1): 18-20, Jan. 1985.
24. BAUER, H.M., HILDESHEIM, A., SCHIFFMAN, M.H., GLASS, A.G., RUSH, B.B., SCOTT, D.R., CADELL, D.M., KURMAN, R.J., and MANOS, M.M. Determinants of genital human papillomavirus infection in low-risk women in Portland, Oregon. *Sexually Transmitted Diseases* 20(5): 274-278, Sep.-Oct. 1993.
25. BBC NEWS. Emergency contraception should be easier to get. BBC News Online [Website]. <[http://news.bbc.co.uk/hi/english/health/newsid\\_368000/368495.stm](http://news.bbc.co.uk/hi/english/health/newsid_368000/368495.stm)>. Jun. 14, 1999. Accessed Mar. 7, 2000.

26. BERAL, V., HERMON, C., KAY, C., HANNAFORD, P., DARBY, S., and REEVES, G. Mortality associated with oral contraceptive use: 25 year follow up of cohort of 46,000 women from Royal College of General Practitioners' oral contraception study. *British Medical Journal* 318(7176): 96-100, Jan. 9, 1999.
27. BERGSTEN, N.A. Clinical efficacy, acceptability and metabolic effects of new low dose combined oral contraceptives. *Acta Obstetrica et Gynecologica Scandinavica* (Suppl. 54): 51-59, 1976.
28. BERGSTEN, N.A. Investigation of a new low-dose oral contraceptive: 30 mcg ethinyl estradiol and 150 mcg levonorgestrel (d-norgestrel). *Clinical Therapeutics* 1(1): 26-32, 1977.
29. BERKOWITZ, G., KELSEY, J., HOLFORD, T., and LIVOLSI, V. Exogenous hormone use and fibrocystic breast disease among pre- and postmenopausal women. Presented at the 16th Annual Meeting of the Society for Epidemiological Research, Winnipeg, Canada, Jun. 15-17. Unpublished, 1983, 6 p.
30. BERMAN, S.M. and HEIN, K. Adolescents and STDs. In: Holmes, K.K., Sparling, P.F., Mårdh, P.A., Lemon, S.M., Stamm, W.E., Piot, P., and Wasserheit, J.N., eds. *Sexually Transmitted Diseases*. 3rd ed. McGraw-Hill, 1999, p. 129-142.
31. BICEGO, G. and AHMAD, O.B. Infant and child mortality. Calverton, Maryland, Macro International, (Demographic and Health Surveys Comparative Studies No. 20) Aug. 1996, 65 p.
32. BILIAN, A. Abortion and emergency contraception: Chinese experience. *Chinese Medical Journal* 110(1): 36-42, Jan. 1997.
33. BLANEY, C. Abused women have special needs. *Network* 18(4): 15-18, Family Health International, Summer 1998.
34. BLOEMENKAMP, K.W., ROSENDAAL, F.R., HELMERHORST, F.M., BULLER, H.R., and VANDENBROUCKE, J.P. Enhancement by factor V Leiden mutation of risk of deep-vein thrombosis associated with oral contraceptives containing a third-generation progestogen. *Lancet* 346(8990): 1593-1596, Dec. 16, 1995.
35. BLUM, M., GILEROVITCH, M., BENAIM, J., and APPELBAUM, T. The correlation between Chlamydia antigen, antibody, vaginal colonization and contraceptive method in young unmarried women. *Advances in Contraception* 6(1): 41-45, Mar. 1990.
36. BOLAN, G., EHRHARDT, A.A., and WASSERHEIT, J.N. Gender perspectives and STDs. In: Holmes, K.K., Sparling, P.F., Mårdh, P.A., Lemon, S.M., Stamm, W.E., Piot, P., and Wasserheit, J.N., eds. *Sexually Transmitted Diseases*. 3rd ed. McGraw-Hill, 1999, p. 117-127.
37. BONITS, I., VAVILIS, D., PANIDIS, D., THEODORIDIS, T., KONSTANTINIDIS, T., and SIDIROPOULOU, A. Detection of *Chlamydia trachomatis* in asymptomatic women: Relationship to history, contraception, and cervicitis. *Advances in Contraception* 10(4): 309-315, Dec. 1994.
38. BORODITSKY, R., FISHER, W., and SAND, M. The 1995 Canadian contraception study. *Journal of the Society of Obstetricians and Gynecologists of Canada* (Special Supplement): 1-31, Dec. 1996.
39. BOUNDS, W., VESSEY, M., and WIGGINS, P. A randomized double-blind trial of two low dose combined oral contraceptives. *British Journal of Obstetrics and Gynecology* 86(4): 325-329, Apr. 1979.
40. BRACKEN, M.B. Oral contraception and congenital malformations in offspring: A review and meta-analysis of the prospective studies. *Obstetrics and Gynecology* 76(3, Pt. 2): 552-557, Sep. 1990.
41. BRAT, T. Clinical trial with a new low oestrogen combined oral contraceptive. *Current Medical Research and Opinion* 2(8): 465-470, 1974.
42. BRIGGS, M. Oestrogen content of oral contraceptives [letter]. *Lancet* 2(8050): 1233, Dec. 10, 1977.
43. BRINTON, L.A. Oral contraceptives and cervical neoplasia. *Contraception* 43(6): 581-595, Jun. 1991.
44. BRINTON, L.A., TASHIMA, K.T., LEHMAN, H.F., LEVINE, R.S., MALLIN, K., SAVITZ, D.A., STOLLEY, P.D., and FRAUMENI, J.F., Jr. Epidemiology of cervical cancer by cell type. *Cancer Research* 47(6): 1706-1711, Mar. 15, 1987.
45. BRINTON, L.A., VESSEY, M.P., FLAVEL, R., and YEATES, D. Risk factors for benign breast disease. *American Journal of Epidemiology* 113(3): 203-214, Mar. 1981.
46. BRISSON, J., MORIN, C., FORTIER, M., ROY, M., BOUCHARD, C., LÉGER, J., CHRISTEN, A., GUIMONT, C., PENAULT, F., and MEISELS, A. Risk factors for cervical intraepithelial neoplasia: Differences between low- and high-grade lesions. *American Journal of Epidemiology* 140(8): 700-710, Oct. 15, 1994.
47. BROCK, K.E., BERRY, G., BRINTON, L.A., KERR, C., MACLENNAN, R., MOCK, P.A., and SHEARMAN, R.P. Sexual, reproductive and contraceptive risk factors for carcinoma-in-situ of the uterine cervix in Sydney. *Medical Journal of Australia* 150(3): 125-130, Feb. 6, 1989.
48. BROOKS, P.G. Pill formulations and their effect on lipid and carbohydrate metabolism. *Journal of Reproductive Medicine* 29(7 Suppl.): 539-546, Jul. 1984.
49. BROWN, S., VESSEY, M., and STRATTON, I. The influence of method of contraception and cigarette smoking on menstrual patterns. *British Journal of Obstetrics and Gynecology* 95(9): 905-910, Sep. 1988.
50. BRUMSTED, J.R. and RIDDICK, D.H. Menstruation and disorders of menstrual function. In: SCOTT, J.R., DISAIA, P.J., MAMMOND, C.B., and SPILLACIA, W.N., eds. *Danforth's Obstetrics and Gynecology*. 7th ed. Philadelphia, J.B. Lippincott Company, 1994, p. 665-679.
51. BURKETT, B.J., PETERSON, C.M., BIRCH, L.M., BRENNAN, C., NUCKOLIS, M.L., WARD, B.E., and CRUM, C.P. The relationship between contraceptives, sexual practices, and cervical human papillomavirus infection among a college population. *Journal of Clinical Epidemiology* 45(11): 1295-1302, Nov. 1992.
52. BURSAUX, E. Santé: Une «pillule du lendemain» est désor-

mais en vente libre dans les pharmacies. *Le Monde édition électronique*. Jun. 24, 1999, 2 p. (Available: <<http://www.lemonde.fr/article/0,2320,12721,00.html>>, Accessed Feb. 14, 2000).

53. BUTTERMORE, S. and NOLAN, C. Six years of clinical experience using postcoital contraception in college women. *Journal of American College Health* 42(2): 61-63, Sep. 1993.
54. BYE, P.G. and ELSTEIN, M. Clinical assessment of a low-estrogen combined oral contraceptive. *British Medical Journal* 2(5863): 389-392, May 19, 1973.
55. CAIRNS, V., KEIL, U., DOERING, A., KOENIG, W., STIEBER, J., and KLEINBAUM, D.G. Oral contraceptive use and blood pressure in a German metropolitan population. *International Journal of Epidemiology* 14(3): 389-395, Sep. 1985.
56. CAMERON, D.W., SIMONSEN, J.D., D'COSTA, L.J., RONALD, A.R., MAITHA, G.M., GAKINYA, M.N., CHEANG, M., NDINYA-ACHOLA, J.O., PIOT, P., and BRUNHAM, R.C. Female to male transmission of Human Immunodeficiency Virus type 1: Risk factors for seroconversion in men. *Lancet* 2(8660): 403-407, Aug. 19, 1989.
57. CAMPODONICO, I., GUERRERO, B., and LANDA, L. Effect of a low-dose oral contraceptive (150 mcg Levonorgestrel and 30 mcg Ethinylestradiol) on lactation. *Clinical Therapeutics* 1(6): 434-459, 1978.
58. CANCER AND STEROID HORMONE STUDY OF THE CENTERS FOR DISEASE CONTROL AND NATIONAL INSTITUTE OF CHILD HEALTH AND HUMAN DEVELOPMENT. Combination oral contraceptive use and the risk of endometrial cancer. *Journal of the American Medical Association* 257(6): 796-800, Feb. 13, 1987.
59. CANCER AND STEROID HORMONE STUDY OF THE CENTERS FOR DISEASE CONTROL AND THE NATIONAL INSTITUTE OF CHILD HEALTH AND HUMAN DEVELOPMENT. The reduction in risk of ovarian cancer associated with oral-contraceptive use. *New England Journal of Medicine* 316(11): 650-655, Mar. 12, 1987.
60. CARDY, G.C. Outcome of pregnancies after failed hormonal postcoital contraception *An interim report*. *British Journal of Family Planning* 21(3): 112-115, Oct. 21, 1995.
61. CAROLE, A., MARINI, C., and DE MATTEIS, G. History of migraine and risk of cerebral ischaemia in young adults. The Italian National Research Council Study Group on Stroke in the Young. *Lancet* 347(9014): 1503-1506, Jun. 1, 1996.
62. CASAGRANDE, J.T., PIKE, M.C., ROSS, R.K., LOUIE, E.W., ROY, S., and HENDERSON, B.E. "Incessant ovulation" and ovarian cancer. *Lancet* 2(8135): 170-174, Jul. 28, 1979.
63. CELENTANO, D.D., AKARASEW, P., SUSSMAN, L., SU-PRASERT, S., MATANASARAWOAT, A., WRIGHT, N.H., THEETRANONT, C., and NELSON, K.E. HIV-1 infection among lower class commercial sex workers, in Chiang Mai, Thailand. *AIDS* 8(4): 533-537, Apr. 1994.
64. CELENTANO, D.D., KLASSEN, A.C., WEISMAN, C.S., and ROSENHEIM, N.B. The role of contraceptive use in cervical cancer: The Maryland Cervical Cancer Case-Control Study. *American Journal of Epidemiology* 126(4): 592-604, Oct. 1987.
65. CENTER FOR REPRODUCTIVE LAW AND POLICY. Emergency contraception advances women's rights. New York, Center for Reproductive Law and Policy, Jul. 1999, 2 p.
66. CENTERS FOR DISEASE CONTROL AND PREVENTION. HIV prevention through early detection and treatment of other sexually transmitted diseases United States. *MMWR* 47(RR-12), Oct. 9, 1998.
67. CERUTI, M., CANESTRELLI, M., CONDEMI, V., PIANTILLI, G., DE PAOLIS, P., AMONE, F., and TOVAGLIARI, D. Methods of contraception and rates of genital infections. *Clinical and Experimental Obstetrics and Gynecology* 21(2): 119-123, 1994.
68. CHAN, W.Y., DAWOOD, M.Y., and FUCHS, F. Prostaglandins in primary dysmenorrhea: Comparison of prophylactic and non-prophylactic treatment with ibuprofen and use of oral contraceptives. *American Journal of Medicine* 70(3): 535-541, Mar. 1981.
69. CHANG, C.L., DONAGHY, M., and POULTER, N. Migraine and stroke in young women: Case-control study. *British Medical Journal* 318(7175): 13-18, Jan. 2, 1999.
70. CHAO, S. The effect of lactation on ovulation and fertility. *Clinic in Perinatology* 14(1): 39-50, Mar. 1987.
71. CHASAN-TABER, L., WILLET, W.C., MANSON, J.E., SPIEGELMAN, D., HUNTER, D.J., CURHAN, G., COLOITZ, G.A., and STAMPFER, M.J. Prospective study of oral contraceptives and hypertension among women in the United States. *Circulation* 94(3): 483-489, Aug. 1, 1996.
72. CHAUDHURY, R.R., CHOMPOOTAWEEP, S., DUSITSIN, N., FRIESEN, H., and TANKEYOON, M. The release of prolactin by medroxyprogesterone acetate in human subjects. *British Journal of Pharmacology* 59(3): 433-434, Mar. 1977.
73. CHAYA, N., HELSING, K., and CONLY, S.R. Contraceptive choice: Worldwide access to family planning [wall chart]. Population Action International, 1996.
74. CHIAFFARINO, F., PARAZZINI, F., LA VECCHIA, C., RICCI, E., and CROSGIAGNI, P. Oral contraceptive use and benign gynecologic conditions: A review. *Contraception* 57(1): 11-18, Jan. 1998.
75. CHILD, T.J., MACKENZIE, I.Z., and REES, M. Terminations of pregnancy, not unplanned deliveries, increased as result of pill scare [letter]. *British Medical Journal* 313(7063): 1005, Oct. 19, 1996.
76. CHILD, T.J., REES, M., and MACKENZIE, I.Z. Pregnancy terminations after oral contraception scare [letter]. *Lancet* 347(9010): 1260-1261, May 4, 1996.
77. CLEMETSON, D.B.A., MOSS, G.B., WILLERFORD, D.M., HENSEL, M., EMONYI, W., HOLMES, K.K., PLUMMER, F., NDINYA-ACHOLA, J., ROBERTS, P.L., HILLIER, S., and KREISS, J.K. Detection of HIV DNA in cervical and vaginal secretions. Prevalence and correlates among women in Nairobi, Kenya. *Jour-*



nal of the American Medical Association 269(22): 2860-2864. Jun. 9, 1993.

78. COHEN, J. Clinical use of biphasic and triphasic pills. International Planned Parenthood Federation Medical Bulletin 19(4): 1-2. Aug. 1985.

79. COHEN, S.A. Objections, confusion among pharmacists threaten access to emergency contraception. The Guttmacher Report on Public Policy 2(3): 1-3. Alan Guttmacher Institute. Jun. 1999.

80. COKER, A.L., MCCANN, M.F., HULKA, B.S., and WALTON, L.A. Oral contraceptive use and cervical intraepithelial neoplasia. Journal of Clinical Epidemiology 45(10): 1111-1118. Oct. 1992.

81. COLLABORATIVE GROUP FOR THE STUDY OF STROKE IN YOUNG WOMEN. Oral contraceptives and stroke in young women: Associated risk factors. Journal of the American Medical Association 231(7): 718-722. Feb. 17, 1975.

82. COLLABORATIVE GROUP ON HORMONAL FACTORS IN BREAST CANCER. Breast cancer and hormonal contraceptives: Collaborative reanalysis of individual data on 53,297 women with breast cancer and 100,239 women without breast cancer from 54 epidemiological studies. Lancet 347(9017): 1713-1727. Jun. 22, 1996.

\*83. COLLABORATIVE GROUP ON HORMONAL FACTORS IN BREAST CANCER. Breast cancer and hormonal contraceptives: Further results. Contraception 54(3 Suppl.): 15-315. Sep. 1996.

\*84. CONFERENCE ON LACTATIONAL AMENORRHEA METHOD FOR FAMILY PLANNING. Consensus statement: Lactational amenorrhea method for family planning. Bellagio, Italy. Unpublished, 1995. 5 p.

85. CONSORTIUM FOR EMERGENCY CONTRACEPTION. Emergency contraceptive pills. A resource packet for health care providers and programme managers. Welcomes, Maryland, Consortium for Emergency Contraception, 1996. 100 p.

86. CONTRACEPTION REPORT. Venous thromboembolism and desogestrel- or gestodene-containing combination oral contraceptives: What are the facts? Contraception Report 7(1): 3-6. Apr. 1996.

87. COOPER, C., HANNAFORD, P., CROFT, P., and KAY, C.R. Oral contraceptive pill use and fractures in women: A prospective study. Bone 14(1): 41-45. Jan/Feb. 1993.

88. CORSON, S.L. Increased risk from third-generation progestogens: Fuzzy logic or fuzzy science? [editorial]. Journal of Reproductive Medicine 41(9): 711-712. Sep. 1996.

89. COWAN, B.D. and MORRISON, J.C. Management of abnormal genital bleeding in girls and women. New England Journal of Medicine 324(24): 1710-1715. Jun. 13, 1991.

90. COY, J.F., MAIR, H., and RATKOWSKY, D.A. Breastfeeding and oral contraceptives: Tasmanian survey. Australian Paediatric Journal 19(3): 168-171. Sep. 1983.

91. CRAIB, K.J., MEDDINGS, D.R., STRATHDEE, S.A., HOGG, R.S., MONTANER, J.S., O'SHAUGHNESSY, M.V., and SCHECHTER, M.T. Rectal gonorrhea as an independent risk factor for HIV infection in a cohort of homosexual men. Genitourinary Medicine 71(3): 150-154. Jun. 1995.

92. CRAMER, D.W., HUTCHISON, G.B., WELCH, W.R., SCULLY, R.E., and KNAPP, R.C. Factors affecting the association of oral contraceptives and ovarian cancer. New England Journal of Medicine 307(17): 1047-1051. Oct. 21, 1982.

\*93. CRITCHLOW, C.W. and KIVIAT, N.B. Old and new issues in cervical cancer control [editorial]. Journal of the National Cancer Institute 91(3): 200-201. Feb. 3, 1999.

94. CRITCHLOW, C.W., WÖLNER-HANSEN, P., ESCHENBACK, D.A., KIVIAT, N.B., KOUTSKY, L.A., STEVENS, C.E., and HOLMES, K.K. Determinants of cervical ectopia and of cervicitis: Age, oral contraception, specific cervical infection, smoking, and douching. American Journal of Obstetrics and Gynecology 173(2): 534-543. Aug. 1995.

\*95. CROFT, P. and HANNAFORD, P.C. Risk factors for acute myocardial infarction in women: Evidence from the Royal College of General Practitioners' Oral Contraception Study. British Medical Journal 298(6667): 165-168. Jan. 21, 1989.

96. CROOK, D., GODSLAND, I.F., and WYNN, V. Oral contraceptives and coronary heart disease: Modulation of glucose tolerance and plasma lipid risk factors by progestins. American Journal of Obstetrics and Gynecology 158(6 Pt. 2): 1612-1620. Jun. 1988.

97. CROWLEY, T., HORNER, P., HUGHES, A., BERRY, J., PAUL, I., and CAUL, O. Hormonal factors and the laboratory detection of *Chlamydia trachomatis* in women: Implications for screening? International Journal of STD and AIDS 8(1): 25-31. Jan. 1997.

98. CROXATTO, H.B., DIAZ, S., PERALTA, O., JUEZ, G., HERREROS, C., CASADO, M.E., SALVATIERRA, A.M., MIRANDA, P., and DURAN, E. Fertility regulation in nursing women: IV. Long-term influence of a low-dose combined oral contraceptive initiated at day 30 postpartum upon lactation and infant growth. Contraception 27(1): 13-25. Jan. 1983.

99. CULLBERG, G., SAMSOE, G., ANDERSEN, R.F., BREDESGAARD, P., ANDERSEN, N.B., ERNEROT, H., FANOE, E., FYLLING, P., HAACK-SØRENSEN, P.E., and KLOTTTRUP, P. Two oral contraceptives, efficacy, serum proteins, and lipid metabolism. A comparative multicentre study on a triphasic and a fixed dose combination. Contraception 26(3): 229-243. Sep. 1982.

100. CULLBERG, J. Mental effects of hormone preparations with varied gestagen doses and constant oestrogen dose as compared to placebo. In: Psychosomatic Medicine in Obstetrics and Gynecology. Basel, Switzerland, Karger. 1972. p. 503-506.

101. DALING, J.R., MADELINE, M.M., MCKINLEY, B., CARTER, J.W., WIFE, G.C., ASHLEY, R., SCHWARTZ, S.M., BECKMANN, A.M., HAGENSEE, M.E., MANDELSON, M.T., and GALLOWAY, D.A. The relationship of human papillomavirus-related cervical tumors to cigarette smoking, oral contraceptive use, and prior herpes simplex virus type 2 infection. Cancer, Epidemiology, Biomarkers and Prevention 5(7): 541-548. Jul. 1996.

102. DALY, S.F., DOYLE, M., ENGLISH, J., TURNER, M., CLINCH,

J., and PRENDIVILLE, W. Can the number of cigarettes smoked predict high-grade cervical intraepithelial neoplasia among women with mildly abnormal cervical smears? American Journal of Obstetrics and Gynecology 179(2): 399-402. Aug. 1998.

\*103. DATEY, S., GAUR, L.N., and SAXENA, B.N. Vaginal bleeding patterns of women using different contraceptive methods (implants, injectables, IUDs, oral pills) in an Indian experience. An ICMR task force study. Contraception 51(3): 155-165. Mar. 1995.

104. D'AVANZO, B., LA VECCHIA, C., NEGRI, E., PARAZZINI, F., and FRANCESCHI, S. Oral contraceptive use and risk of myocardial infarction: An Italian case-control study. Journal of Epidemiology and Community Health 48(3): 324-325. Jun. 1994.

105. DAWOOD, M.Y. Dysmenorrhea. Clinical Obstetrics and Gynecology 33(1): 168-178. Mar. 1990.

106. DAWSON, D.A. Trends in use of oral contraceptives Data from the 1987 National Health Interview Survey. Family Planning Perspectives 22(4): 169-172. Jul/Aug. 1990.

107. DE SANJOSÉ, S., BOSCH, F.X., MUÑOZ, N., and SHAH, K. Social differences in sexual behaviour and cervical cancer. In: Kogevinas, M., Pearce, N., Susser, M., and Booffetta, P., eds. Social Inequalities and Cancer. Vol. 138. Lyon, International Agency for Research on Cancer, p. 309-317.

108. DE VINCENTI, I. and EUROPEAN STUDY GROUP ON HETEROSEXUAL TRANSMISSION OF HIV. A longitudinal study of Human Immunodeficiency Virus transmission in heterosexual partners. New England Journal of Medicine 331(6): 341-346. Aug. 11, 1994.

\*109. DECHERNEY, A. Bone-sparing properties of oral contraceptives. American Journal of Obstetrics and Gynecology 174(Part 1): 15-20. Jan. 1996.

110. DELBANCO, D.F., MAULDON, J., and SMITH, M.D. Little knowledge and limited practice: Emergency contraceptive pills, the public, and the obstetrician-gynecologist. Obstetrics and Gynecology 89(6): 1006-1011. Jun. 1997.

111. DELGADO BETANCOURT, J., SANDOVAL, J.C., SANCHEZ, F., VALLESTERO DE CANO, P., De la LUZ BANTISTA, M., and JIMENEZ, F. Influence of Exluton (progestogen-only OC) and the Multiload Cu 250 IUD on lactation. Contraceptive Delivery Systems 5(2): 91-95. Apr. 1984.

112. DELGADO-RODRIGUEZ, M., SILLERO-ARENAS, M., MARTIN-MORENO, I.M., and GALVEZ-VARGAS, R. Oral contraceptives and cancer of the cervix uteri. A meta-analysis. Acta Obstetrica et Gynecologica Scandinavica 71(5): 368-376. Jul. 1992.

113. DERMAN, R. Oral contraceptives: Assessment of benefits. Journal of Reproductive Medicine 31(9 Suppl.): 879-886. Sep. 1986.

114. DESCHAMPS, M.M., PAPE, J.W., HAFNER, A., and JOHNSON Jr., W.D. Heterosexual transmission of HIV in Haiti. Annals of Internal Medicine 125(4): 324-330. Aug. 15, 1996.

115. DESMARES, J., BARY, M., VITTECOQ, D., GROFFE, S., and BACH, J.F. Feature of HIV epidemic in women among a Parisian cohort (abstract no. M.C.3248). 7th International Conference on AIDS, Florence, Italy, Jun. 16-21, 1991.

\*116. DIAZ, S., PERALTA, O., JUEZ, G., HERREROS, C., CASADO, M.E., SALVATIERRA, A.M., MIRANDA, P., DURAN, E., and CROXATTO, H.B. Fertility regulation in nursing women: III. Short-term influence of a low-dose combined oral contraceptive upon lactation and infant growth. Contraception 27(1): 1-11. Jan. 1983.

117. DICKEY, R.P. Managing Contraceptive Pill Patients. 8th ed. Durant, Oklahoma, Essential Medical Information Systems, 1994. 303 p.

118. DILLNER, L. Pill scare linked to rise in abortions. British Journal of Medicine 312(7037): 996. Apr. 20, 1996.

119. DIONNE, P. and VICKERSON, F. A double-blind comparison of two oral contraceptives containing 50 mcg and 30 mcg ethinyl estradiol. Current Therapeutic Research, Clinical and Experimental 16(4): 281-288. Apr. 1974.

120. DJERASSI, C. The Politics of Contraception. New York, Norton, 1979. 274 p.

121. DORFLINGER, L.J. Relative potency of progestins used in oral contraceptives. Contraception 31(6): 557-570. Jun. 1985.

122. DUNN, N., THOROGOOD, M., FARAGHER, B., de CAESTECKER, L., MACDONALD, T., MCCOLLUM, C., THOMAS, S., and MANN, R. Oral contraceptives and myocardial infarction: Results of the MICA case-control study. British Medical Journal 318(7198): 1579-1584. Jun. 12, 1999.

123. ELLERTSON, C., TRUSSELL, J., STEWART, F.H., and WINIKOFF, B. Should emergency contraceptive pills be available without prescriptions? Journal of the American Medical Women's Association 53(5 Suppl. 2): 226-229, 232. 1998.

124. ELLIS, J.W. Multiphasic oral contraceptives: Efficacy and metabolic impact. Journal of Reproductive Medicine 32(1): 28-36. Jan. 1987.

125. ELLSWORTH, H. Focus on triphasil. Journal of Reproductive Medicine 31(6 Suppl.): 559-564. Jun. 1986.

126. ENG, T.R. and BUTLER, W.T., eds. The Hidden Epidemic: Confronting Sexually Transmitted Diseases. Washington, D.C., National Academy Press, 392 p. 1997.

127. ENZELSBERGER, H., METKA, M., HEYTMANEK, G., SCHURZ, B., KURZ, C., and KUSZTRICH, M. Influence of oral contraceptive use on bone density in climacteric women. Maturitas 9(4): 375-378. 1988.

128. EUROPEAN STUDY GROUP. Risk factors for male to female transmission of HIV. British Medical Journal 298(6671): 411-415. Feb. 18, 1989.

\*129. EXPERT PANEL ON EMERGENCY CONTRACEPTION. Consensus statement on emergency contraception. Bellagio, Italy, South to South Cooperation in Reproductive Health, May 15, 1995. (Bellagio Conference on Emergency Contraception) 8 p.

130. FAMILY HEALTH INTERNATIONAL (FHI). Benefits and risks of combined oral contraceptives. Research Triangle Park, North Carolina, FHI, 1994. 2 p.

\*131. FARLEY, T.M., COLLINS, J., and SCHLESSELMAN, J.J. Hormo-

nal contraception and risk of cardiovascular disease: An international perspective. Contraception 57(3): 211-230. Mar. 1998.

132. FARMER, R.D., LAWRENSEN, R.A., THOMPSON, C.R., KENNEDY, J.G., and HAMBLETON, I.R. Population-based study of risk of venous thromboembolism associated with various oral contraceptives. Lancet 349(9045): 83-88. Jan. 11, 1997.

133. FARRELL, B., SOLTER, C., and HUBER, D. Comprehensive reproductive health and family planning training curriculum: Module 5: Emergency contraceptive pills. Pathfinder International (Website). <http://www.pathfind.org/html/mod\_links.htm>. Nov. 1997. Accessed Mar. 7, 2000.

134. FAY, R.A. Failure with the new triphasic oral contraceptive Logynon. British Medical Journal 284(6308): 17-18. Jan. 2, 1982.

\*135. FERNANDEZ, E., LA VECCHIA, C., FRANCESCHI, S., BRAGA, C., TALAMINI, R., NEGRI, E., and PARAZZINI, F. Oral contraceptive use and risk of colorectal cancer. Epidemiology 9(3): 295-300. May 1998.

136. FINER, L.B. and ZABIN, L.S. Does the timing of the first family planning visit still matter? Family Planning Perspectives 30(1): 30-33. 42. Jan/Feb. 1998.

137. FISCH, I.R. and FRANK, J. Oral contraceptives and blood pressure. Journal of the American Medical Association 237(23): 2499-2503. Jun. 6, 1977.

138. FISCH, I.R., FREEDMAN, S.H., and MYATT, A.V. Oral contraceptives, pregnancy, and blood pressure. Journal of the American Medical Association 222(12): 1507-1510. Dec. 18, 1972.

139. FORMAN, D., VINCENT, T.J., and DOLL, R. Cancer of the liver and the use of oral contraceptives. British Medical Journal 292(6532): 1359-1361. May 24, 1986.

140. FOSS, G.L. and FOTHERBY, K. Low-oestrogen combined oral contraceptive. Acta Europaea Fertilitatis 4(2): 57-58. Jun. 1973.

141. FOSS, G.L. and FOTHERBY, K. Clinical trial of a low dose combined oral contraceptive ("Ovranette"). Current Medical Research and Opinion 3(2): 12-16. 1975.

142. FOSTER, D.C. Low-dose monophasic and multiphasic oral contraceptives: A review of potency, efficacy, and side effects. Seminars in Reproductive Endocrinology 7(3): 205-212. Aug. 1989.

143. FOTHERBY, K. Metabolic effects of low dose combined oral contraceptives. British Journal of Family Planning 10(1): 15-19. Apr. 1984.

144. FRANCESCHI, S., LA VECCHIA, C., and TALAMINI, R. Oral contraceptives and cervical neoplasia: Pooled information from retrospective and prospective epidemiologic studies. Tumori 72(1): 21-30. Feb. 28, 1986.

145. FRASER, I.S. A review of the use of progestogen-only minipills for contraception during lactation. Reproduction, Fertility and Development 3(3): 245-254. 1991.

146. FRASER, I.S. and JANSEN, R.P. Why do inadvertent pregnancies occur in oral contraceptive users? Effectiveness of oral contraceptive regimens and interfering factors. Contraception 27(6): 531-551. Jun. 1983.

\*147. FRASSINELLI-GUNDERSON, E.P., MARGEN, S., and BROWN, J.R. Iron stores in users of oral contraceptive agents. American Journal of Clinical Nutrition 41(4): 703-712. Apr. 1985.

148. FURNER, S.E., DAVIS, F.G., NELSON, R.L., and HAENSZEL, W. A case-control study of large bowel cancer and hormone exposure in women. Cancer Research 49(17): 4936-4940. Sep. 1, 1989.

149. GALVÃO, L., DÍAZ, J., DÍAZ, M., OSIS, M.J., CLARK, S., and ELLERTSON, C. Emergency contraception: Knowledge, attitudes and practices among Brazilian obstetrician-gynecologists. International Family Planning Perspectives 25(4): 168-171. 180. Dec. 1999.

150. GARDNER, M.B. Facts about oral contraceptives. Washington D.C., Government Printing Office, 1984. 19 p.

151. GARDNER, R. and BLACKBURN, R. People who move: New reproductive health focus. Population Reports, Series J, No. 45. Baltimore, Johns Hopkins School of Public Health, Population Information Program, Nov. 1996. 28 p.

152. GARG, S.K., CHASE, H.P., MARSHALL, G., HOOPS, S.L., HOLMES, D.L., and JACKSON, W.E. Oral contraceptives and renal and retinal complications in young women with insulin-dependent diabetes mellitus. Journal of the American Medical Association 271(14): 1099-1102. Apr. 13, 1994.

153. GASPARD, U.J. Metabolic effects of oral contraceptives. American Journal of Obstetrics and Gynecology 157(4 Pt. 2): 1029-1041. Oct. 1987.

154. GASPARD, U.J., DEVILLE, J.L., and DUBOIS, M. Clinical experience with triphasic oral contraceptive ("Trinordiol") in young women. Current Medical Research and Opinion 8(6): 395-404. 1983.

155. GASPARD, U.J., DUBOIS, M., GILLAIN, D., FRANCHI-MONT, P., and DUUVIER, J. Ovarian function is effectively inhibited by a low-dose triphasic oral contraceptive containing ethinylestradiol and levonorgestrel. Contraception 29(4): 305-318. Apr. 1984.

156. GASPARD, U.J. and LEFEBVRE, P.J. Clinical aspects of the relationship between oral contraceptives, abnormalities in carbohydrate metabolism, and the development of cardiovascular disease. American Journal of Obstetrics and Gynecology 163(1 Pt. 2): 334-343. Jul. 1990.

157. GICHANGI, P.B., KARANJA, J.G., KIGONDU, C.S., FONCK, K., and TEMMERMAN, M. Knowledge, attitudes, and practices regarding emergency contraception among nurses and nursing students in two hospitals in Nairobi, Kenya. Contraception 59(4): 253-256. Apr. 1999.

158. GILLESPIE, M., NOTELOVITZ, M., ELINGSON, A.B., and KHAN, F.Y. Effect of long-term triphasic oral contraceptive use on glucose tolerance and insulin secretion. Obstetrics and Gynecology 78(1): 108-114. Jul. 1991.

159. GITSCH, G., KAINZ, C., STUDNICKA, M., REINTHALLER, A., TATRA, G. and BREITENECKER, G. Oral contraceptives and



- human papillomavirus infection in cervical intraepithelial neoplasia. *Archives of Gynecology and Obstetrics* 252: 25-30, 1992.
160. GLASIER, A. Safety of emergency contraception. *Journal of the American Medical Women's Association* 53(Suppl. 2): 219-221, 1998.
161. GLOSS, B., BERNARD, H.U., and SEEDORF, K. The upstream regulatory region of the human papillomavirus-16 contains an E2 protein-independent enhancer which is specific for cervical carcinoma cells and regulated by glucocorticoid hormones. *EMBO Journal* 6(12): 3735-3743, Dec. 1, 1987.
162. GODSLAND, I.F., CROOK, D., DEVENPORT, M., and WYNN, V. Relationships between blood pressure, oral contraceptive use and metabolic risk markers for cardiovascular disease. *Contraception* 52(3): 143-149, Sep. 1995.
163. GOLDBAUM, G.M., KENDRICK, J.S., HOGEJUN, G.C., and GENTRY, E.M. The relative impact of smoking and oral contraceptive use on women in the United States. *Journal of the American Medical Association* 258(10): 1339-1342, Sep. 11, 1987.
164. GOLDSMITH, N.F., and JOHNSTON, J.O. Bone mineral effects of oral contraceptives, pregnancy, and lactation. *Journal of Bone and Joint Surgery* 57-A(5): 657-668, Jul. 1975.
165. GOODYEAR, L., and MCGINN, T. Emergency contraception among refugees and the displaced. *Journal of the American Medical Women's Association* 53(Suppl. 2): 266-270, 1998.
166. GRAHAM, C.A., and SHERWIN, B.B. A prospective treatment study of premenstrual symptoms using a triphasic oral contraceptive. *Journal of Psychosomatic Research* 36(3): 257-66, Apr. 1992.
167. GRAHAM, H. Failure with the new triphasic oral contraceptive Logynon [letter]. *British Medical Journal* 284(6313): 422, Feb. 6, 1982.
168. GRAM, I.T., AUSTIN, H., and STALSBERG, H. Cigarette smoking and the incidence of cervical intraepithelial neoplasia, grade III, and cancer of the cervix uteri. *American Journal of Epidemiology* 135(4): 341-346, Feb. 15, 1992.
169. GRAM, I.T., MACALUSO, M., and STALSBERG, H. Oral contraceptive use and the incidence of cervical intraepithelial neoplasia. *American Journal of Obstetrics and Gynecology* 167(1): 40-44, Jul. 1992.
170. GREFF, R.O. The biological history of the pill. In: Parnham, M.I. and BRUINVELS, J., eds. *Discoveries in Pharmacology*. Vol. 2. Amsterdam, Elsevier Science Publishers, 1984, p. 321-337.
171. GRICE, D., VILLARD-MACKINTOSH, L., YEATES, D., and VESSEY, M. Oral contraceptives and diabetes mellitus. *British Journal of Family Planning* 17(2): 39-40, Jul. 1991.
172. GRIMES, D.A. Dispelling OC myths and misperceptions. *Dialogues in Contraception* 4(3): 1-4, Summer 1994.
173. GRIMES, D.A., and ECONOMY, K.E. Primary prevention of gynecologic cancers. *American Journal of Obstetrics and Gynecology* 172(1 Pt. 1): 227-235, Jan. 1995.
174. GRIMES, D.A., and RAYMOND, E.G. Bundling a pregnancy test with the Yuzpe regimen of emergency contraception. *Obstetrics and Gynecology* 94(3): 471-473, Sep. 1999.
175. GROU, F., and RODRIGUES, I. The morning-after pill—How long after? *American Journal of Obstetrics and Gynecology* 171(6): 1529-1534, Dec. 1994.
176. GUERREIRO, D., GIGANTE, M.A.M., and TELES, C.E. Sexually transmitted diseases and reproductive tract infections among contraceptive users. *International Journal of Gynecology and Obstetrics* 63(Suppl. 1): S167-S173, Dec. 1, 1998.
177. GUILLEBAUD, I. *The Pill*. 2nd ed. London, Oxford University Press, 1983, 278 p.
178. GUILLEBAUD, I. Practical prescribing of the combined oral contraceptive pill. Unpublished, 1989, 25 p.
179. GUILLEBAUD, I. *The Pill and Other Forms of Hormonal Contraception*. 5th ed. Oxford, Oxford University Press, 1997, 320 p.
180. GWINN, M.L., LEE, N.C., RHODES, P.H., LAYDE, P.M., and RUBIN, G.L. Pregnancy, breast feeding, and oral contraceptives and the risk of epithelial ovarian cancer. *Journal of Clinical Epidemiology* 43(6): 559-568, 1990.
181. HAMMOND, C., and BACHUS, K. Ectopic pregnancy. In: Scott, J., Disaia, P., Hammond, C., and Spellacy, W., eds. *Danforth's Obstetrics and Gynecology*. 7th ed. 1984.
182. HAMMOND, P.B. Reporting pill panic. A comparative analysis of media coverage of health scares about oral contraceptives. *British Journal of Family Planning* 23(2): 62-66, Jul. 1997.
183. HANNAFORD, P.C. Cervical cancer and methods of contraception. *Advances in Contraception* 7(4): 317-324, Dec. 1991.
184. HANNAFORD, P.C. Combined oral contraceptives: Do we know all of their effects? *Contraception* 51(6): 325-327, Jun. 1995.
185. HANNAFORD, P.C., and KAY, C.R. Oral contraceptives and diabetes mellitus. *British Medical Journal* 299(6711): 1315-1316, Nov. 25, 1989.
186. HARPER, C., and ELLERTSON, C. The emergency contraceptive pill: An inquiry on knowledge and attitudes. Princeton, New Jersey, Princeton University, Center of Domestic and Comparative Policy Studies, Jan. 1994, 36 p.
187. HARRISON, M. Morning-after pill available over the counter. *PA News wire service*, Jan. 7, 2000.
188. HASSAN, E.O., EL-NAHAL, M., ROUSHDY, M.G., and EL-HOUSINI, M. IUD use dynamics in Egypt. Cairo, Egyptian Fertility Care Society and Population Council, 1994, 411 p.
189. HATCHER, R.A., and GUILLEBAUD, I. The pill: Combined oral contraceptives. In: Hatcher, R.A., Trussell, J., Stewart, F., Cates Jr., W., Stewart, G.K., Guest, F., and Kowal, D. *Contraceptive Technology*. 17th ed. New York, Ardent Media, 1998, p. 405-466.
190. HATCHER, R.A., RINEHART, W., BLACKBURN, R., and GELLER, J.S. *The Essentials of Contraceptive Technology*. Baltimore, Johns Hopkins School of Public Health, Population Information Program, Jul. 1997, 340 p.
191. HEINEMANN, L.A., DOMINH, T., GUGGENMOOS-HOLZMANN, I., THIEL, C., and GARBE, E. Oral contraceptives and liver cancer: Results of the Multicentre International Liver Tumor Study (MILTS). The Collaborative MILTS Project Team. *Contraception* 56(5): 275-284, Nov. 1997.
192. HEINEMANN, L.A., LEWIS, M.A., SPITZER, W.O., THORGOOD, M., GUGGENMOOS-HOLZMANN, I., and BRUPPACHER, R. Thromboembolic stroke in young women: A European case-control study on oral contraceptives. *Contraception* 57(1): 29-37, Jan. 1998.
193. HEISE, L., ELLSBERG, M., and GOTTMOELLER, M. Ending violence against women. *Population Reports*, Series L, No. 11. Baltimore, Johns Hopkins School of Public Health, Population Information Program, Dec. 1999, 43 p.
194. HELMERHORST, F.M., BLOEMENKAMP, K.W., ROSENDAAL, F.R., and VANDENBROUCKE, J.P. Oral contraceptives and thrombotic disease: Risk of venous thromboembolism. *Thrombosis and Haemostasis* 78(1): 327-333, Jul. 1997.
195. HENDERSON, B.E., CASAGRANDE, J.T., PIKE, M.C., MACK, T., ROSARIO, I., and DUKE, A. The epidemiology of endometrial cancer in young women. *British Journal of Cancer* 47(6): 749-756, Jun. 1983.
196. HENDERSON, B.E., PRESTON-MARTIN, S., EDMONDSON, H.A., PETERS, R.L., and PIKE, M.C. Hepatocellular carcinoma and oral contraceptives. *British Journal of Cancer* 48(3): 437-440, Sep. 1983.
197. HENRY, A. Saga of the newer generation pills and the concept of risk. *Reproductive Health Matters* 7(7): 158-161, May 1996.
198. HILDESHEIM, A., REEVES, W.C., BRINTON, L.A., LAVERY, C., BRENES, M., De La GUARDIA, M.E., GODOY, J., and RAWLS, W.E. Association of oral contraceptive use and human papillomaviruses in invasive cervical cancers. *International Journal of Cancer* 45(5): 860-864, May 15, 1990.
199. HILDESHEIM, A., SCHIFFMAN, M.H., GRAVITT, P.E., GLASS, A.G., GREER, C.E., ZHANG, T., SCOTT, D.R., RUSH, B.B., LAWLER, P., SHERMAN, M.E., KURMAN, R.J., and MANOS, M.M. Persistence of type-specific human papillomavirus infection among cytologically normal women. *Journal of Infectious Diseases* 169(2): 235-240, Feb. 1994.
200. HILDRETH, N.G., KELSEY, J.L., LIVOLSI, V.A., FISCHER, D.B., HOLFORD, T.R., MOSTOW, E.D., SCHWARTZ, P.E., and WHITE, C. An epidemiologic study of epithelial carcinoma of the ovary. *American Journal of Epidemiology* 114(4): 398-405, Sep. 1981.
201. HILLIER, S., and HOLMES, K.K. Bacterial vaginosis. In: Holmes, K.K., Sparling, P.F., Mårdh, P.-A., Lemon, S.M., Stamm, W.E., Piot, P., and Wasserheit, J.N., eds. *Sexually Transmitted Diseases*. 3rd ed. McGraw-Hill, p. 563-586, 1999.
202. HITTI, J., WALKER, C.K., NSUBUGA, P.S., GRANT, R.M., TAGER, I.B., and MBIDDE, E.K. Oral contraceptive use and HIV infection [abstract no. PoC 4309]. 8th International Conference on AIDS, Amsterdam, Jul. 19-24, 1992.
203. HO, G.Y.F., BIERMAN, R., BEARDSLEY, L., CHANG, C.J., and BURK, R.D. Natural history of cervicovaginal papillomavirus infection in young women. *New England Journal of Medicine* 338(7): 423-428, Feb. 12, 1998.
204. HOFFMAN, J. The morning-after pill: A well-kept secret. *New York Times Magazine*, Jan. 10, 1993, pp. 12-15, 30, 32.
205. HOLMBERG, S.D., STEWART, J.A., GERBER, A.R., BYERS, R.H., LEE, F.K., O'MALLEY, P.M., and NAHMIAS, A.J. Prior herpes simplex virus type 2 infection as a risk factor for HIV infection. *Journal of the American Medical Association* 259(7): 1048-1050, Feb. 19, 1988.
206. HOLOWATY, P., MILLER, A.B., ROHAN, T., and TO, T. Natural history of dysplasia of the uterine cervix. *Journal of the National Cancer Institute* 91(3): 252-258, Feb. 3, 1999.
207. HOLT, V.L., DALING, J.R., MCKNIGHT, B., MOORE, D., STERGACHIS, A., and WEISS, N.S. Functional ovarian cysts in relation to the use of monophasic and triphasic oral contraceptives. *Obstetrics and Gynecology* 79(4): 529-533, Apr. 1992.
208. HUBER, D.H., KHAN, A.R., BROWN, K., MALAKAR, M., and WAIT, G. Oral and injectable contraceptives: The effects on breast-milk and child growth in Bangladesh. Presented at the International Workshop on Research Frontiers in Fertility Regulation in Mexico City, Feb. 11-14, 1980. Unpublished, 22 p.
209. HUGHES, I. An open assessment of a new low dose oestrogen combined oral contraceptive. *Journal of International Medical Research* 6(1): 41-45, 1978.
210. HULKA, B.S., CHAMBLESS, L.E., KAUFMAN, D.G., FOWLER Jr., W.C., and GREENBERG, B.G. Protection against endometrial carcinoma by combination-product oral contraceptives. *Journal of the American Medical Association* 247(4): 475-477, Jan. 22-29, 1982.
211. HULE, V.J. The effects of hormonal contraceptives on lactation: Current findings, methodological considerations, and future priorities. *Studies in Family Planning* 12(4): 134-155, Apr. 1981.
212. HUTCHINGS, J., WINKLER, J.L., FULLER, T.S., GARDNER, J.S., WELLS, E.S., DOWNING, D., and SHAFER, R. When the morning after is Sunday: Pharmacist prescribing of emergency contraceptive pills. *Journal of the American Medical Women's Association* 53(Suppl. 2): 230-232, 1998.
213. INAMAN, W.H. Oral contraceptives and fatal subarachnoid haemorrhage. *British Medical Journal* 216(5203): 1468-1470, Dec. 8, 1979.
214. INMAN, W.H., VESSEY, M.P., WESTERHOLM, B., and ENGELUND, A. Thromboembolic disease and the steroid content of oral contraceptives: A report to the committee on the safety of drugs. *British Medical Journal* 25(703): 203-209, Apr. 25, 1970.
215. INTERNATIONAL AGENCY FOR RESEARCH ON CANCER (IARC). Human papillomavirus vaccines and their potential use in the prevention and treatment of cervical cancer. IARC (Website). <http://www.iarc.fr/paperroot/RELEASES/108E.HTM>. Jun. 7, 1995. Accessed Mar. 7, 2000.
216. INTERNATIONAL AGENCY FOR RESEARCH ON CANCER (IARC). IARC Monographs programme on the evaluation of carcinogenic risks to humans: Human papillomavirus (HPV). IARC (Website). <http://1193.511.1164.11/indexes/monographs/Vol64/>
- HPV.htm>. Dec. 15, 1994. Accessed Mar. 7, 2000.
217. INTERNATIONAL MEDICAL ADVISORY PANEL, I. Highlights of IMAP's September meeting. International Planned Parenthood Federation (Website). <http://www.ippf.org/imap/ming9709.htm>. Sep. 8-10, 1997. Accessed Mar. 7, 2000.
218. IVERSEN, O.E., and NILSEN, S.T. The recent pill scare and number of legal abortions in Norway. *Acta Obstetrica et Gynecologica Scandinavica* 75(7): 690-691, Aug. 1996.
219. JACOBSON, D.L., PERALTA, L., GRAHAM, N.M.H., and ZENILMAN, J. Development of cervical ectopy: Epidemiology and meta-analysis of the relationship of ectopy and oral contraceptives to the risk of chlamydial infection. Doctor of Philosophy Dissertation, Department of Epidemiology, Johns Hopkins University School of Hygiene and Public Health, Baltimore, 1999, 53 p.
220. JHPiECo (JOHNS HOPKINS PROGRAM FOR INTERNATIONAL EDUCATION IN REPRODUCTION HEALTH). Cervical cancer prevention. JHPiECo (Website). <http://www.jhpiego.jhu.edu/SPECIAL/CERCAN/CERCAN.HTM>. Jan. 28, 2000. Accessed Mar. 7, 2000.
221. JICK, H., JICK, S.S., GUREWICH, V., MYERS, M.W., and VASILAKIS, C. Risk of idiopathic cardiovascular death and nonfatal venous thromboembolism in women using oral contraceptives with differing progestogen components. *Lancet* 346(8990): 1589-1593, Dec. 16, 1995.
222. JICK, H., JICK, S.S., MYERS, M.W., and VASILAKIS, C. Risk of acute myocardial infarction and low-dose combined oral contraceptives [letter]. *Lancet* 347(9001): 627-628, Mar. 2, 1996.
223. JICK, H., JICK, S.S., MYERS, M.W., and VASILAKIS, C. Third-generation oral contraceptives and venous thrombosis [letter]. *Lancet* 349(9053): 731-732, Mar. 8, 1997.
224. JICK, H., PORTER, J., and ROTHMAN, K.J. Oral contraceptives and nonfatal stroke in healthy young women. *Annals of Internal Medicine* 89(1): 58-60, Jul. 1978.
225. JOHNSON, S.R. The epidemiology and social impact of premenstrual symptoms. *Clinical Obstetrics and Gynecology* 30(2): 367-376, Jun. 1987.
226. JOSEPH, J. Get your prescription for morning-after pills in advance: Don't wait until the condom breaks. ABC News wire service. 1998, p. 2. (Available: [http://more.abcnws.go.com/sections/living/HealthyWoman/healthywoman\\_17.html](http://more.abcnws.go.com/sections/living/HealthyWoman/healthywoman_17.html)). Accessed Mar. 7, 2000.
227. JUDD, H.L., and MELDRUM, D.R. Physiology and pathophysiology of menstruation and menopause. In: Romney, S.L., Gray, M.J., Little, A.B., Merrill, J.A., QUILLIGAN E.J., and Stander, R.W. *Gynecology and Obstetrics: The Health Care of Women*. 2nd ed. New York, McGraw Hill, 1981, p. 885-907.
228. JUDD, S.J., and KERIN, J. Contraception and diabetes mellitus. *Clinical Reproduction and Fertility* 4(5): 297-304, Oct. 1986.
229. KAISER FAMILY FOUNDATION (KFF). Emergency contraception: Still 'America's best kept secret'? [Knight Ridder/Kansas City Star]. KFF Daily Reproductive Health Report. Sep. 16, 1999. (Available: <http://report.kff.org/archive/repro/1999/09/kf990916.4.html>). Accessed Mar. 7, 2000.
230. KAISER FAMILY FOUNDATION (KFF). India: Widespread support for over-the-counter EC. [The Hindu]. KFF Daily Reproductive Health Report. Oct. 29, 1999. (Available: <http://report.kff.org/archive/repro/1999/10/kf991029.9.html>). Accessed Mar. 3, 2000.
231. KAISER FAMILY FOUNDATION (KFF). Japan: Does hesitate to prescribe emergency contraception. [Japan Times]. KFF Daily Reproductive Health Report. Jun. 25, 1999. (Available: <http://report.kff.org/archive/repro/1999/06/kf990625.7.html>). Accessed Mar. 3, 2000.
232. KASLER, W.J., ZENILMAN, J.M., ERICKSON, B., FOX, R., PETERMAN, T.A., and E.W.III, H. Serconversion in patients attending sexually transmitted disease clinics. *AIDS* 8(3): 351-355, Mar. 1994.
233. KATAJA, V., SYRJÄNEN, S., YLISKOSKI, M., HIPPELÄINEN, M., VÄYRYNEN, M., SAARIKOSKI, S., MÄNTYJÄRVI, R., JOKEA, V., SALONEN, J.T., and SYRJÄNEN, K. Risk factors associated with cervical human papillomavirus infections: A case-control study. *American Journal of Epidemiology* 138(9): 735-745, Nov. 1, 1993.
234. KAUFMAN, D.W., SHAPIRO, S., SLOAN, D., ROSENBERG, L., MIETTINEN, O.S., STOLLEY, P., KNAPP, R.C., LEAVITT JR., T., WATRING, W.G., and ROSENHEIM, N.B. Decreased risk of endometrial cancer among oral-contraceptive users. *New England Journal of Medicine* 303(18): 1045-1047, Oct. 30, 1980.
235. KAUFMAN, R.H., and ADAM, E. Is human papillomavirus testing of value in clinical practice? *American Journal of Obstetrics and Gynecology* 180(5): 1049-1053, May 1999.
236. KELSEY, J.L., LIVOLSI, V.A., HOLFORD, T.R., FISCHER, D.B., MOSTOW, E.D., SCHWARTZ, P.E., O'CONNOR, T., and WHITE, C. A case-control study of cancer of the endometrium. *American Journal of Epidemiology* 116(2): 333-342, Aug. 1982.
237. KENNEDY, K.I., RIVERA, R., and MCNEILLY, A.S. Consensus statement on the use of breastfeeding as a family planning method, Bellagio, Italy, Aug. 1988. *Contraception* 39(5): 477-496, May 1989.
238. KESSLER, D.A. Communicating with patients about their medications. *New England Journal of Medicine* 352(23): 1650-1652, Dec. 5, 1991.
239. KETTING, E. The relative reliability of oral contraceptives: Findings of an epidemiologic study. *Contraception* 37(4): 343-348, Apr. 1988.
240. KEW, M.C., SONG, E., MOHAMMED, A., and HODKINSON, J. Contraceptive steroids as a risk factor for hepatocellular carcinoma: A case-control study in South African black women. *Hepatology* 11(2): 298-302, Feb. 1990.
241. KHAW, K.T., and PEARF, W.S. Blood pressure and contraceptive use. *British Medical Journal* 285(6339): 403-407, Aug. 7, 1982.
242. KIMANI, J., MACLEAN, I.W., BWAYO, J.I., MACDONALD, K., OYUGI, J., MAITHA, C.M., PEELING, R.W., CHEANG, M.,



- NAGELKERKE, N.J., and PLUMMER, F.A. Risk factors for *Chlamydia trachomatis* pelvic inflammatory disease among sex workers in Nairobi, Kenya. *Journal of Infectious Diseases* 173(6): 1437-1444. Jun. 1996.
243. KING, R.J. Biology of female sex hormone action in relation to contraceptive agents and neoplasia. *Contraception* 43(6): 527-542. Jun. 1991.
244. KIVIAT, N.B., KOUTSKY, L.A., and PAAVONEN, J. Cervical neoplasia and other STD-related genital tract neoplasias. In: Holmes, K.K., Sparling, P.F., Mårdh, P.-A., Lemon, S.M., Stamm, W.E., Piot, P., and Wasserheit, J.N., eds. *Sexually Transmitted Diseases*. 3rd ed. McGraw-Hill. 1999. p. 811-831.
245. KJÆR, S.K., ENGHOLM, G., DAHL, C., BOCK, J.E., LYNCE, E., and JENSEN, O.M. Case-control study of risk factors for cervical squamous cell neoplasia in Denmark. III. Role of oral contraceptive use. *Cancer Causes and Control* 4(6): 513-519. Nov. 1993.
- \*246. KJOS, S.L., PETERS, R.K., XIANG, A., THOMAS, D., SCHAEFER, U., and BUCHANAN, T.L. Contraception and the risk of type 2 diabetes mellitus in Latina women with prior gestational diabetes mellitus. *Journal of the American Medical Association* 280(6): 533-538. Aug. 12, 1998.
- \*247. KLEERKOPPER, M., BRIENZA, R.S., SCHULTZ, L.R., and JOHNSON, C.C. Oral contraceptive use may protect against low bone mass. *Archives of Internal Medicine* 151(10): 1971-1976. Oct. 1991.
248. KOETSAWANG, S., and SRISUPANIDIT, S. Clinical trial of low-dose oral contraceptive pill containing 0.75 mg. lynestrol and 0.0375 mg. ethinyl estradiol. *Journal of the Asian Federation of Obstetrics and Gynecology* 5(4): 28-32. Jul. 1977.
249. KREISS, J., WILLERFORD, D.M., HENSEL, M., EMOYI, W., PLUMMER, F., NDINYA-ACHOLA, J., ROBERTS, P.L., HOSKYN, J., HILLIER, S., KIVIAT, N., and HOLMES, K.K. Association between cervical inflammation and cervical shedding of human immunodeficiency virus DNA. *Journal of Infectious Diseases* 170(6): 1597-1601. Dec. 1994.
- \*250. KRITZ-SILVERSTEIN, D., and BARRETT-CONNOR, E. Bone mineral density in postmenopausal women as determined by prior oral contraceptive use. *American Journal of Public Health* 83(1): 100-102. Jan. 1993.
251. KRUGER-KJÆR, S., VAN DEN BRULE, A.J., SVARE, E.I., ENGHOLM, G., SHERMAN, M.E., POLL, P.A., WALBOOMERS, J.M., BOCK, J.E., and MEIJER, C.J. Different risk factor patterns for high-grade intraepithelial lesions on the cervix among HPV-positive and HPV-negative young women. *International Journal of Cancer* 76(5): 613-619. May 29, 1998.
252. KUNE, G.A., KUNE, S., and WATSON, L.F. Oral contraceptive use does not protect against large bowel cancer. *Contraception* 41(1): 19-25. Jan. 1990.
253. KUTNER, S.J., and BROWN, W.L. Types of oral contraceptives, depression, and premenstrual symptoms. *Journal of Nervous and Mental Disease* 155(3): 153-162. Sep. 1972.
- \*254. LA VECCHIA, C., NEGRI, E., and PARAZZINI, F. Oral contraceptives and primary liver cancer. *British Journal of Cancer* 59(3): 460-461. Mar. 1989.
- \*255. LABBOK, M., COONEY, K., and COLY, S. Guidelines: Breast-feeding, family planning, and the lactational amenorrhea method-LAM. Washington D.C., Georgetown University, Institute for Reproductive Health, 1994. 18 p.
256. LAGA, M., MANOKA, A., KIVUVU, M., MALELE, B., TULIZA, M., NZILA, N., GOEMAN, J., BEHETS, F., BATTER, V., ALARY, M., HEYWARD, W.L., RYDER, R.W., and PIOT, P. Non-ulcerative sexually transmitted diseases as risk factors for HIV-1 transmission in women: Results from a cohort study. *AIDS* 7(1): 95-102. Jan. 1993.
257. LANCET. Pill scares and public responsibility [editorial]. *Lancet* 347(9017): 1707. Jun. 22, 1996.
- \*258. LANES, S.F., BIRMANN, B., WALKER, A.M., and SINGER, S. Oral contraceptive type and functional ovarian cysts. *American Journal of Obstetrics and Gynecology* 166(3): 956-961. Mar. 1992.
259. LANGER, A., HARPER, C., GARCIA-BARRIOS, C., SCHIAVON, R., HEIMBURGER, A., ELUL, B., DELGADO, S.R., and ELLERTSON, C. Emergency contraception in Mexico City: What do health care providers and potential users know and think about it? *Contraception* 60(4): 233-241. Oct. 1999.
- \*260. LARSSON, G., MILSOM, I., LINDSTEDT, G., and RYBO, G. The influence of a low-dose combined oral contraceptive on menstrual blood loss and iron status. *Contraception* 46(4): 327-334. Oct. 1992.
261. LAUTMANN, R., and STARKE, K. GERMANY. In: Francoeur, R.T., ed. *The International Encyclopedia of Sexuality*. Vol. 1. New York, Continuum. 1997. p. 492-518.
262. LAWSON, J.S., YULIANO, S.E., PASQUALE, S.A., and OSTERMAN, J.J. Optimum dosage of an oral contraceptive: A report from the study of seven combinations of norgestimate and ethinyl estradiol. *American Journal of Obstetrics and Gynecology* 174(3): 315-320. Jun. 1, 1997.
263. LAYDE, P.M., BERAL, V., and KAY, C.R. Further analyses of mortality in oral contraceptive users: Royal College of General Practitioners' Oral Contraception Study. *Lancet* 1(8219): 541-546. Mar. 7, 1971.
264. LAYDE, P.M., ORY, H.W., BERAL, V., and KAY, C.R. Incidence of arterial disease among oral contraceptive users. *Royal College of General Practitioners' Oral Contraception Study*. *Journal of the Royal College of General Practitioners* 33(247): 75-82. Feb. 1983.
265. LEES, A.W., BURNES, P.E., and GRACE, M. Oral contraceptives and breast disease in premenopausal northern Albertan women. *International Journal of Cancer* 22(6): 700-707. Dec. 15, 1978.
266. LEUNG, W.C., LEUNG, T.W., LAM, Y.Y., and HO, P.C. The prevalence of domestic violence against pregnant women in a Chinese community. *International Journal of Gynecology and Obstetrics* 66(1): 23-30. Jul. 1999.
- \*267. LEWIS, M.A., HEINEMANN, L.A., MACRAE, K.D., BRUP-
- PACHER, R., and SPITZER, W.O. The increased risk of venous thromboembolism and the use of third generation progestogens: Role of bias in observational research. *Contraception* 54(1): 5-13. Jul. 1996.
- \*268. LEWIS, M.A., HEINEMANN, L.A., SPITZER, W.O., MACRAE, K.D., and BRUPPACHER, R. The use of oral contraceptives and the occurrence of acute myocardial infarction in young women. Results from the Transnational Study on Oral Contraceptives and the Health of Young Women. *Contraception* 56(3): 129-140. Sep. 1997.
- \*269. LEWIS, M.A., and SPITZER, W.O. The role of bias in observational studies on oral contraceptives [letter]. *Contraception* 55(3): 192-194. Mar. 1997.
- \*270. LEWIS, M.A., SPITZER, W.O., HEINEMANN, L.A., MACRAE, K.D., BRUPPACHER, R., and THOROGOOD, M. Third generation oral contraceptives and risk of myocardial infarction: An international case-control study. *British Medical Journal* 312(7023): 88-90. Jan. 13, 1996.
271. LEY, C., BAUER, H.M., REINGOLD, A., SCHIFFMAN, M.H., CHAMBERS, J.C., TASHIRO, C.J., and MANOS, M.M. Determinants of genital human papillomavirus infection in young women. *Journal of the National Cancer Institute* 83(14): 997-1003. Jul. 17, 1991.
- \*272. LIDEGAARD, O. Oral contraception and risk of a cerebral thromboembolic attack: Results of a case-control study. *British Medical Journal* 306(6883): 956-963. Apr. 10, 1993.
- \*273. LIDEGAARD, O. Oral contraceptives, pregnancy and the risk of cerebral thromboembolism: The influence of diabetes, hypertension, migraine and previous thrombotic disease. *British Journal of Obstetrics and Gynaecology* 102(2): 153-159. Feb. 1995.
- \*274. LIDEGAARD, O., and KREINER, S. Oral contraceptives, pregnancy and the risk of cerebral thromboembolism: The influence of diabetes, hypertension, migraine and previous thrombotic disease. Authors' reply [letter]. *British Journal of Obstetrics and Gynaecology* 103(1): 94. Jan. 1996.
- \*275. LIDEGAARD, O., and MILSOM, I. Oral contraceptives and thrombotic diseases: Impact of new epidemiological studies [editorial]. *Contraception* 53(3): 135-139. Mar. 1996.
276. LIES, E. At long last, the pill goes on sale in Japan. (Tokyo). Reuters wire service. Sep. 2, 1999.
277. LINDGREN, A., and OLSSON, R. Liver damage from low-dose oral contraceptives. *Journal of Internal Medicine* 234(3): 287-292. Sep. 1993.
278. LINDSAY, R., TOHME, J., and KANDERS, B. The effect of oral contraceptive use on vertebral bone mass in pre- and post-menopausal women. *Contraception* 34(4): 333-340. Oct. 1986.
279. LITTA, P., AGNELLO, A., and AZZENA, A. HPV genital infections and contraception. 19: 136-138. 1992.
280. LOBO, R.A. Lipids, clotting factors, and diabetes: Endogenous risk factors for cardiovascular disease. *American Journal of Obstetrics and Gynecology* 158(6 Pt. 2): 1584-1591. Jun. 1988.
281. LONGSTRETH Jr., W.T., KOEPEL, T.D., YERBY, M.S., and VAN BELLE, G. Risk factors for subarachnoid hemorrhage. *Stroke* 16(3): 377-385. May/Jun. 1985.
282. LONGSTRETH Jr., W.T., and SWANSON, P.D. Oral contraceptives and stroke. *Stroke* 15(4): 747-750. Jul/Aug. 1984.
283. LÖRINCZ, A.T., SCHIFFMAN, M.H., JAFFURS, W.J., MARLOW, J., QUINN, A.P., and TEMPLE, G.F. Temporal associations of human papillomavirus infection with cervical cytologic abnormalities. *American Journal of Obstetrics and Gynecology* 162(3): 645-651. Mar. 1990.
284. LOUV, W.C., AUSTIN, H., PERLMAN, I., and ALEXANDER, W.J. Oral contraceptive use and the risk of chlamydia and gonococcal infections. *American Journal of Obstetrics and Gynecology* 160(2): 396-402. Feb. 1989.
285. MALOTTE, C.K., WIESMEIER, E., and GELINEAU, K.J. Screening for chlamydial cervicitis in a sexually active university population. *American Journal of Public Health* 80(4): 469-471. Apr. 1990.
286. MANN, J.I. Oral contraceptives and myocardial infarction in young women: A further report. *British Medical Journal* 3(5984): 631-632. Sep. 1975.
287. MANN, J.I., DOLL, R., THOROGOOD, M., VESSEY, M.P., and WATERS, W.E. Risk factors for myocardial infarction in young women. *British Journal of Preventive and Social Medicine* 30(2): 94-100. Jun. 1976.
288. MANN, J.I., and INMAN, W.H. Oral contraceptives and death from myocardial infarction. *British Medical Journal* 2(5965): 245-248. May 3, 1975.
289. MANN, J.I., INMAN, W.H., and THOROGOOD, M. Oral contraceptive use in older women and fatal myocardial infarction. *British Medical Journal* 2(6033): 445-447. Aug. 21, 1976.
290. MANN, J.I., VESSEY, M.P., THOROGOOD, M., and DOLL, R. Myocardial infarction in young women with special reference to oral contraceptive practice. *British Medical Journal* 2(5965): 241-245. May 3, 1975.
291. MARTIN Jr., H.L., NYANGE, P.M., JACKSON, D.J., MANDALIYA, K., HOLMES, K.K., NGUGI, E., NDINYA-ACHOLA, J.O., PLUMMER, F., and KREISS, J.K. Risk factors for HIV seroconversion in commercial sex workers in Mombasa, Kenya: Role of hormonal contraception and STDs (abstract no. 394C). 10th International Conference on AIDS, 10, No. 2. Yokohama, Japan, Aug. 7-12, 1994.
292. MARTIN, S.L., KILGALLAN, B., TSUI, A.O., MAITRA, K., SINGH, K.K., and KUPPER, L.L. Sexual behaviors and reproductive health outcomes: Associations with wife abuse in India. *Journal of the American Medical Association* 282(20): 1967-1972. Nov. 24, 1999.
- \*293. MARTINEZ, M.E., GRODSTEIN, E., GIOVANNUCCI, E., COLDITZ, G.A., SPEIZER, F.E., HENNEKENS, C., ROSNER, B., WILLETT, W.C., and STAMPER, M.J. A prospective study of reproductive factors, oral contraceptive use, and risk of colorectal cancer. *Cancer Epidemiology, Biomarkers and Prevention* 6(1): 1-5. Jan. 1997.
294. MASSIL, H.Y., and O'BRIEN, P.M. Approach to the management of premenstrual syndrome. *Clinical Obstetrics and Gynecology* 30(2): 443-452. Jun. 1987.
295. MASTROIANNI Jr., L. Noncontraceptive benefits of oral contraceptive agents. Patients should know the positive effects. *Postgraduate Medicine* 93(1): 193-197. Jan. 1993.
296. MCCANN, M.F., LISKIN, L., PIOTROW, P.T., RINEHART, W., and FOX, G. Breast-feeding, fertility, and family planning. *Population Reports, Series J, No. 24*. Baltimore, Johns Hopkins School of Public Health, Population Information Program, Mar. 1984. 52 p.
- \*297. MCCANN, M.F., and POTTER, L.S. Progestin-only oral contraception: A comprehensive review. *Contraception* 50(Suppl. 1): S9-S195. Dec. 1994.
298. MCCAULEY, A.P., and SALTER, C. Meeting the needs of young adults. *Population Reports, Series J, No. 41*. Baltimore, Johns Hopkins School of Public Health, Population Information Program, Oct. 1995. 44 p.
299. MCGOWAN, L., PARENT, L., LEDNAR, W., and NORRIS, H.J. The woman at risk for developing ovarian cancer. *Gynecologic Oncology* 7(3): 325-344. Jun. 1979.
300. MEADE, T.W., CHAKRABARTI, R., HAINES, A.P., HOWARTH, D.J., NORTH, W.R., and STIRLING, Y. Haemostatic, lipid, and blood-pressure profiles of women on oral contraceptives containing 50 mcg or 30 mcg of oestrogen. *Lancet* 2(8045): 948-951. Nov. 5, 1977.
301. MEADE, T.W., GREENBER, G., and THOMPSON, S.G. Progestogens and cardiovascular reactions associated with oral contraceptives and a comparison of the safety of 50- and 30-mcg oestrogen preparations. *British Medical Journal* 280(6224): 1157-1161. May 10, 1980.
302. MEARS, E., and GRANT, E.C. "Anovlar" as an oral contraceptive. *British Medical Journal* 1: 111. 1961.
303. MEHENDALE, S.M., RODRIGUES, J.J., BROOKMEYER, R.S., GANGAKHEDKAR, R.R., DIVEKAR, A.D., GOKHALE, M.R., RISBUD, A.R., PARANJPE, R.S., SHEPHARD, M.E., and ROMPALO, A.E. Incidence and predictors of Human Immunodeficiency Virus type 1 seroconversion in patients attending sexually transmitted disease clinics in India. *Journal of Infectious Diseases* 172(6): 1486-1491. Dec. 1995.
304. MEIRIK, O., and BENAGIANO, G. Twenty years of epidemiology in fertility regulation. *Epidemiology and Public Health* 44(6): 577-587. Nov. 1996.
305. MESTMAN, J.H., and SCHMIDT-SAROSI, C. Diabetes mellitus and fertility control: Contraception management issues. *American Journal of Obstetrics and Gynecology* 168(6 Pt. 2): 2012-2020. Jun. 1993.
306. MILLS, A.M., WILKINSON, C.L., BROMHAM, D.R., ELIAS, J., FOTHERBY, K., GUILLEBAUD, J., KUBBA, A., and WADE, A. Guidelines for prescribing combined oral contraceptives. *British Medical Journal* 312(7023): 121-122. Jan. 13, 1996.
- \*307. MILMAN, N., KIRCHHOFF, M., and JØRGENSEN, T. Iron status markers, serum ferritin and hemoglobin in 1359 Danish women in relation to menstruation, hormonal contraception, parity, and postmenopausal hormone treatment. *Annals of Hematology* 65(2): 96-102. Aug. 1992.
308. MILSOM, I., and ANDERSSON, B. Effect of various oral contraceptive combinations on dysmenorrhea. *Gynecologic and Obstetric Investigation* 17(6): 284-292. Jun. 1984.
- \*309. MILSOM, I., SUNDELL, G., and ANDERSSON, B. The influence of different combined oral contraceptives on the prevalence and severity of dysmenorrhea. *Contraception* 42(5): 497-506. Nov. 1990.
310. MOI, H. Prevalence of bacterial vaginosis and its association with genital infections, inflammation, and contraceptive methods in women attending sexually transmitted disease and primary health clinics. *International Journal of STD and AIDS* 1(2): 86-94. Mar. 1990.
311. MOOS, R.H. Psychological aspects of oral contraceptives. *Archives of General Psychiatry* 19(1): 87-94. Jul. 1968.
- \*312. MORENO, L., and GOLDMAN, N. Contraceptive failure rates in developing countries: Evidence from the Demographic and Health Surveys. *International Family Planning Perspectives* 17(2): 44-49. Jun. 1991.
313. MORIGI, E.M., and PASQUALE, S.A. Clinical experience with a low dose oral contraceptive containing norethisterone and ethinyl oestradiol. *Current Medical Research and Opinion* 5(8): 655-662. 1978.
314. MOSS, G.B., CLEMETSON, D., I, D.C., PLUMMER, F.A., NDINYA-ACHOLA, J.O., REILLY, M., HOLMES, K.K., PIOT, P., MAITHA, G.M., HILLIER, S.L., KIVIAT, N.C., CAMERON, C.W., WAMOLA, I.A., and KREISS, J.K. Association of cervical ectopy with heterosexual transmission of Human Immunodeficiency Virus: Results of a study of couples in Nairobi, Kenya. *Journal of Infectious Diseases* 164(3): 588-591. Sep. 1991.
315. MOSTAD, S.B., OVERBAUGH, J., DEVANGE, D.M., WELCH, M.J., CHOCHAN, B., MANDALIYA, K., NYANGE, P., MARTIN Jr., H.L., NDINYA-ACHOLA, J., BWAYO, J.J., and KREISS, J.K. Hormonal contraception, vitamin A deficiency, and other risk factors for shedding of HIV-1 infected cells from the cervix and vagina. *Lancet* 350(9082): 922-927. Sep. 27, 1999.
316. MUIA, E., ELLERTSON, C., LUKHANDO, M., ELUL, B., CLARK, S., and OLENIA, J. Emergency contraception in Nairobi, Kenya: Knowledge, attitudes and practices among policymakers, family planning providers and clients, and university students. *Contraception* 60(4): 223-232. Oct. 1999.
317. MUNOZ, N., and BOSCH, F.X. Cervical cancer and human papillomavirus: Epidemiological evidence and perspectives for prevention. *Salud Pública de México* 39(4): 274-282. Jul/Aug. 1997.
- \*318. MURRAY, E.E., LOGAN, R.F., HANNAFORD, P.C., and KAY, C.R. Cigarette smoking and parity as risk factors for the development of symptomatic gall bladder disease in women: results of the



- Royal College of General Practitioners' oral contraception study. *Gut* 35(1): 107-111. Jan. 1994.
319. NAGACHINTA, T., DUERR, A., GARGIULO, P.M., YUTABUTRA, Y., WANNARAT, A., TOVANABUTRA, S., SENAN, S., SURIVANON, V., and DE BOER, M. HIV infectivity by contraceptive method from a partner study in northern Thailand (abstract no. Mo.C.572). 11th International Conference on AIDS, Vancouver, Canada, Jul. 7-12, 1996.
320. NAKIEWICZ, K., GRANIERO, G.R., ESTE, D., MATTAREI, M., ZONZIN, P., and PALATINI, P. Ambulatory blood pressure in mild hypertensive women taking oral contraceptives: A case-control study. *American Journal of Hypertension* 8(3): 249-253. Mar. 1995.
321. NATIONAL INSTITUTES OF HEALTH (NIH) CONSENSUS PANEL ON CERVICAL CANCER. Cervical Cancer. NIH Consensus Statement No. 102. NIH (Website). <<http://isis.nlm.nih.gov/nih/cd/c/www/102text.html>>. 1996. Accessed Mar. 7, 2000.
322. NDUNA, S., and GOODYEAR, L. Pain too deep for tears: Assessing the prevalence of sexual and gender violence among Burundian refugees in Tanzania. *International Rescue Committee*, Sep. 1997. 26 p. (Available: <<http://www.intrescom.org/health/sgviol.html>>. Accessed Mar. 7, 2000).
323. NEGRINI, B.P., SCHIFFMAN, M.H., KURMAN, R.J., BARNES, W., LANNOM, L., MALLEY, K., BRINTON, L.A., DELGADO, G., JONES, S., TCHABO, J.-C., and LANCASTER, W.D. Oral contraceptive use, human papillomavirus infection, and risk of early cytological abnormalities of the cervix. *Cancer Research* 50: 4670-4675. 1990.
324. NEUBERGER, J., FORMAN, D., DOLL, R., and WILLIAMS, R. Oral contraceptives and hepatocellular carcinoma. *British Medical Journal* 292(6532): 1355-1357. May 24, 1986.
325. NEWHOUSE, M.L., PEARSON, R.M., FULLERTON, J.M., BOESEN, E.A., and SHANNON, H.S. A case control study of carcinoma of the ovary. *British Journal of Preventive and Social Medicine* 31(3): 148-153. Sep. 1977.
326. NGOC, N.T.N., ELLERSTON, C., SURASRANG, Y., and LOC, L.T. Knowledge and attitudes about emergency contraception among health workers in Ho Chi Minh City, Vietnam. *International Family Planning Perspectives* 23(2): 68-72. Jun. 1997.
327. NICHOLS, M., ROBINSON, G., BOUNDS, W., NEWMAN, B., and GUILLEBAUD, J. Effect of four combined oral contraceptives on blood pressure in the pill-free interval. *Contraception* 47(4): 367-376. Apr. 1993.
328. NILSSON, L., and SOLVELL, L. Clinical studies on oral contraceptives: A randomized, double-blind, crossover study of 4 different preparations (Anovular mite, Lyndil mite, Ovulen, and Volidan). *Acta Obstetrica et Gynecologica Scandinavica* 46(Suppl. 8): 1-31. 1967.
329. NILSSON, S., MELLBIN, T., HOFVANDER, Y., SUNDELIN, C., VALENTIN, J., and NYGREN, K.G. Long-term follow-up of children breast-fed by mothers using oral contraceptives. *Contraception* 34(5): 443-457. Nov. 1986.
330. NZILA, N., LAGA, M., THIAM, M.A., MAYIMONA, K., EDIDI, B., VAN DYCK, E., BEHETS, F., HASSIG, S., NELSON, A., MOKWA, K., ASHLEY, R.L., PIOT, P., and RYDER, R.W. HIV and other sexually transmitted diseases among female prostitutes in Kinshasa. *AIDS* 5(6): 715-721. Jun. 1991.
331. OH, M.K., FEINSTEIN, R.A., SOILEAU, E.J., CLOUD, G.A., and PASS, R.F. *Chlamydia trachomatis* cervical infection and oral contraceptive use among adolescent girls. *Journal of Adolescent Health Care* 10(5): 376-381. Sep. 1989.
332. OLDFIELD, K., MILNE, R., and VESSEY, M. The effects on mortality of the use of combined oral contraceptives. *British Journal of Family Planning* 24(1): 2-6. Apr. 1998.
333. ORME, M., and BACK, D.J. Oral contraceptive steroids—Pharmacological issues of interest to the prescribing physician. *Advances in Contraception* 7(4): 325-331. Dec. 1991.
334. ORY, H. Functional ovarian cysts and oral contraceptives: Negative association confirmed surgically. *Journal of the American Medical Association* 228(1): 68-69. Apr. 1, 1974.
335. ORY, H., COLE, P., MACMAHON, B., and HOOVER, R. Oral contraceptives and reduced risk of benign breast diseases. *New England Journal of Medicine* 294(8): 419-422. Feb. 19, 1976.
336. ORY, H.W. Ectopic pregnancy and intrauterine contraceptive devices: New perspectives. *Obstetrics and Gynecology* 57(2): 137-144. Feb. 1981.
337. ORY, H.W., FORREST, J.D., and LINCOLN, R. Making choices: Evaluating the health risks and benefits of birth control methods. New York, Alan Guttmacher Institute, 1983. 72 p.
338. OTSEA, K. Prioritizing reproductive health for refugees. *Initiatives in Reproductive Health Policy* 3(1): 1-3. Ips. Sep. 1999.
339. OTTEN, M.W., ZAIDI, A.A., PETERMAN, T.A., ROLFS, R.T., and WITTE, J.J. High rate of HIV seroconversion among patients attending urban sexually transmitted disease clinics. *AIDS* 8(4): 549-553. Apr. 1994.
340. PAAVONEN, J., and LEHTINEN, M. Chlamydial pelvic inflammatory disease. *Human Reproduction Update* 2(6): 519-529. 1996.
341. PAIGE, K.E. Effects of oral contraceptives on affective fluctuations associated with the menstrual cycle. *Psychosomatic Medicine* 33(6): 515-537. Nov/Dec. 1971.
342. PALMER, J.R., ROSENBERG, L., KAUFMAN, D.W., WARSHAUER, M.E., STOLLEY, P., and SHAPIRO, S. Oral contraceptive use and liver cancer. *American Journal of Epidemiology* 130(5): 878-882. Nov. 1989.
343. PALOMO, I., GREBE, G., FERRADA, M., CARRASCO, J.M., MAFFIOLETTI, M., and FELIX, E. Efecto del uso prolongado de dispositivos intrauterinos y anticonceptivos orales, sobre la nutrición del hierro. [SPA] [Effects of the prolonged use of intrauterine devices (IUDs) and oral contraceptives on iron nutrition]. *Revista Medica de Chile* 121(6): 639-644. Jun. 1993.
344. PARAZZINI, F., CHATENOL, L., LA VECCHIA, C., CHIAFFARINO, F., RICCI, E., and NEGRI, E. Time since last use of oral contraceptives and risk of invasive cervical cancer. *European Journal of Cancer* 34(6): 884-888. May 1998.
345. PARAZZINI, F., LA VECCHIA, C., NEGRI, E., BOCCIOLONE, L., FEDELE, L., and FRANCESCHI, S. Oral contraceptive use and the risk of ovarian cancer: An Italian case-control study. *European Journal of Cancer* 27(5): 594-598. May 1991.
346. PARAZZINI, F., LA VECCHIA, C., NEGRI, E., and MAGGI, R. Oral contraceptive use and invasive cervical cancer. *International Journal of Epidemiology* 19(2): 259-263. Jun. 1990.
347. PARK, B.J., STERGACHIS, A., SCHOLDES, D., HEINDRICH, F.E., HOLMES, K.K., and STAMM, W.E. Contraceptive methods and the risk of *Chlamydia trachomatis* infection in young women. *American Journal of Epidemiology* 142(7): 771-778. Oct. 1, 1995.
348. PARKIN, D.M., PISANI, P., and FERLAY, J. Estimates of the worldwide incidence of 25 major cancers in 1990. *International Journal of Cancer* 80(6): 827-841. Mar. 15, 1999.
349. PASQUALE, S.A. Rationale for a triphasic oral contraceptive. *Journal of Reproductive Medicine* 29(7 Suppl.): 560-567. Jul. 1984.
350. PATER, M.M., HUGHES, G.A., HYSLOP, D.E., NAKSHATRI, H., and PATER, A. Glucocorticoid-dependent oncogenic transformation by type 16 but not type 11 human papillomavirus DNA. *Nature* 335(6193): 832-835. Oct. 27, 1988.
351. PERALTA, O., DIAZ, S., JUEZ, G., HERREROS, C., CASADO, M.E., SALVATIERRA, A.M., MIRANDA, P., DURAN, E., and CROXATTO, H.B. Fertility regulation in nursing women: V. Long-term influence of a low-dose combined oral contraceptive initiated at day 90 postpartum upon lactation and infant growth. *Contraception* 27(1): 27-38. Jan. 1983.
352. PEREIRA, A., and JONES, K.P. Oral contraceptives: exploring the benefits, dispelling the myths. *Health and Sexuality* 5(1): 1, 3-5. 16. Fall 1996.
353. PETITTI, D.B., SIDNEY, S., and QUESENBERRY, C.P. Oral contraceptives and myocardial infarction. *Contraception* 57(3): 143-155. Mar. 1998.
354. PETITTI, D.B., SIDNEY, S., QUESENBERRY, C.P., and BERNSTEIN, A. Incidence of stroke and myocardial infarction in women of reproductive age. *Stroke* 28(2): 280-283. Feb. 1997.
355. PETITTI, D.B., and WINGERD, J. Use of oral contraceptives, cigarette smoking, and risk of subarachnoid haemorrhage. *Lancet* 2(8083): 234-236. Jul. 29, 1978.
356. PHARMACIA AND UPJOHN. International survey reveals vast differences in women's use and attitudes about birth control. (Salvador de Bahia, Brazil). PR Newswire wire service. May 6, 1999.
357. PIAGGIO, G., VON HERTZEN, H., GRIMES, D.A., and VAN LOOK, P.F.A. Research letters: Timing of emergency contraception with levonorgestrel or the Yuzpe regimen. *Lancet* 353(9154): 721. Feb. 27, 1999.
358. PIEGSA, K., and GUILLEBAUD, J. Oral contraceptives and the risk of DVT. *Practitioner* 240(1566): 544, 546, 550-551. Sep. 1996.
359. PIKE, M.C. Fertility and its effects on health. In: Digory, P., Potts, M., and Teper, S. *Natural Human Fertility: Social and Biological Determinants*. London, MacMillan Press, 1987. p. 161-189.
360. PIKE, M.C., and SPICER, D.V. Oral contraceptives and cancer. In: Shoupe, D. and Haseltine, F.P., eds. *Oral Contraceptives*. New York, Springer-Verlag, 1993. p. 67-84.
361. PIOTROW, P.T., and LEE, C.M. Oral contraceptives: Fifty million users. *Population Reports*, Series A, No. 1. Baltimore, Johns Hopkins School of Public Health, Population Information Program, Apr. 1974. 28 p.
362. PLOURDE, P.J., PLUMMER, F.A., PEPIN, J., AGOKI, E., MOSS, G., OMBETTE, J., RONALD, A.R., CHEANG, M., D'OSTA, L., and NDINYA-ACHOLA, J.O. Human Immunodeficiency Virus type 1 infection in women attending a sexually transmitted diseases clinic in Kenya. *Journal of Infectious Diseases* 166(1): 86-92. Jul. 1992.
363. PLUMMER, F.A., SIMONSEN, J.N., CAMERON, D.W., NDINYA-ACHOLA, J.O., KREISS, J.K., GAKINYA, M.N., WAIYAKI, P., CHEANG, M., PIOT, P., RONALD, A.R., and NGUGI, E.N. Cofactors in male-female sexual transmission of Human Immunodeficiency Virus type 1. *Journal of Infectious Diseases* 163(2): 233-239. Feb. 1991.
364. POTTER, J.D., and MCMICHAEL, A.J. Large bowel cancer in women in relation to reproductive and hormonal factors: A case-control study. *Journal of the National Cancer Institute* 71(4): 703-709. Oct. 1983.
365. POTTER, L.S. How effective are contraceptives? The determination and measurement of pregnancy rates. *Obstetrics and Gynecology* 88(3 Suppl.): 135-235. Sep. 1996.
366. POULTER, N.R., CHANG, C.L., FARLEY, T.M., MEIRIK, O., and MARMOT, M.G. Venous thromboembolic disease and combined oral contraceptives: Results of international multicentre case-control study. *World Health Organization Collaborative Study of Cardiovascular Disease and Steroid Hormone Contraception*. *Lancet* 346(8990): 1575-1582. Dec. 16, 1995.
367. POULTER, N.R., CHANG, C.L., FARLEY, T.M., MEIRIK, O., and MARMOT, M.G. Ischaemic stroke and combined oral contraceptives: Results of an international, multicentre, case-control study. *WHO Collaborative Study of Cardiovascular Disease and Steroid Hormone Contraception*. *Lancet* 348(9026): 498-505. Aug. 24, 1996.
368. POULTER, N.R., CHANG, C.L., MARMOT, M., FARLEY, T.M., and MEIRIK, O. Third-generation oral contraceptives and venous thrombosis [letter]. *Lancet* 349(9053): 732. Mar. 8, 1997.
369. PRESTON, S.N. A report of a collaborative dose-response clinical study using decreasing doses of combination oral contraceptives. *Contraception* 6(1): 17-35. Jul. 1972.
370. PRINCETON UNIVERSITY OFFICE OF POPULATION RESEARCH. Study aims to broaden available EC regimens. *Princeton University (Website)*. <<http://ec.princeton.edu:80/news/popounc.html>>. Oct. 14, 1999. Accessed Mar. 7, 2000.
371. PROGRAM FOR APPROPRIATE TECHNOLOGY IN HEALTH (PATH). Triphasic OCs: How do they compare with low-dose monophasic OCs? *Outlook* 8(2): 2-5. Seattle, Washington, PATH, Jun. 1990.
372. PROGRAM FOR APPROPRIATE TECHNOLOGY IN HEALTH (PATH). Preventing cervical cancer in low-resource settings. *Outlook* 16(1): 9 p. Seattle, Washington, PATH, May 1998. (Available: <<http://www.path.org/outlook/html/16-1.htm>>. Accessed Mar. 7, 2000).
373. PRSIC, J., and KICOVIC, P.M. Preliminary experience with a new low-oestrogen content combined oral contraceptive. *Current Medical Research and Opinion* 2(4): 204-210. 1974.
374. RAHM, V.A., ODIND, V., and PETERSSON, R. *Chlamydia trachomatis* in sexually active teenage girls: Factors related to genital chlamydial infection: A prospective study. *Genitourinary Medicine* 67(4): 317-321. Aug. 1991.
375. RAMCHARAN, S., PELLEGRIN, F.A., RAY, R., and HSU, J.P. The Walnut Creek Contraceptive Drug Study: A prospective study of the side effects of oral contraceptives. Vol. 3: An interim report—A comparison of disease occurrence leading hospitalization or death in users and nonusers of oral contraceptives. Bethesda, Maryland, U.S. Department of Health and Human Services, National Institute of Child Health and Human Behavior, Jan. 1981. 349 p.
376. RAMSAY, S. UK "pill scare" led to abortion increase. *Lancet* 347(9008): 1109. Apr. 20, 1996.
377. RANDLE, N. Antibiotic- and anticonvulsant-induced oral contraceptive failure. *Journal of Pharmacy Technology* 1(6): 246-249. Nov-Dec. 1985.
378. RAVENHOLT, R.T., and PIOTROW, P.T. Use of oral contraceptives in developing countries. *Pakistan Journal of Medical Research* 8(3): 213-241. Jul. 1969.
379. RAVENHOLT, R.T., PIOTROW, P.T., and SPEIDEL, J.J. Use of oral contraceptives: A decade of controversy. *International Journal of Gynecology and Obstetrics* 8(6): 941-955. Nov. 1970.
380. RAYMOND, E.G. (Family Health International) (Vomiting and ECPs) Personal communication, Feb. 7, 2000.
381. RAYMOND, E.G., CREININ, M.D., BARNHART, K.T., LOV-VORN, A.E., ROUNTREE, W., and TRUSSELL, J. Mefenazine for prevention of nausea associated with emergency contraceptive pills: A randomized trial. *Obstetrics and Gynecology* 95(2): 271-277. Feb. 2000.
382. RICE-WRAY, E., SCHULZ-CONTRERAS, M., GUERRERO, I., and ARANDA-ROSELL, A. Long-term administration of norethindrone in fertility control. *Journal of the American Medical Association* 180(5): 355-358. May 5, 1962.
383. RICHART, R.M., MASOOD, S., SYRJÄNEN, K.J., VASSILAKOS, P., KAUFMAN, R.H., MEISELS, A., OLSZEWSKI, W.T., SAKAMOTO, A., STOLER, M.H., VOIJS, G.P., and WILBUR, D.C. Human papillomavirus. *International Academy of Cytology Task Force summary. Diagnostic Cytology Towards the 21st Century: An International Expert Conference and Tutorial. Acta Cytologica* 42(1): 50-58. Jan/Feb. 1998.
384. RICHART, R.B. Cervical neoplasia: Past, present, and future. *Contemporary OB/GYN* 43 (25th Anniversary Issue): 117-132. May 15, 1998.
385. RIMM, E.B., MANSON, J.E., STAMPER, M.J., COLDITZ, G.A., WILLET, W.C., ROSNER, B., HENNEKEN, C.H., and SPEIZER, F.E. Oral contraceptive use and the risk of Type 2 (non-insulin-dependent) diabetes mellitus in a large prospective study of women. *Diabetologia* 35(10): 967-972. Oct. 1992.
386. RISCH, H.A., MARRETT, L.D., and HOWE, G.R. Parity, contraception, infertility, and the risk of epithelial ovarian cancer. *American Journal of Epidemiology* 140(7): 585-597. Oct. 1, 1994.
387. RIVERA, R., ALMONTE, H., ARREOLA, M., LOPEZ, F., MONARREZ, G., NAVARRO, C., ORTIZ, E., PERKIN, G.W., and RUIZ, R. The effects of three different regimens of oral contraceptives and three different intrauterine devices on the levels of hemoglobin, serum iron and iron binding capacity in anemic women. *Contraception* 27(3): 311-327. Mar. 1983.
388. ROSENBERG, L., KAUFMAN, D.W., HELMRICH, S.P., MILLER, O.R., STOLLEY, P.D., and SHAPIRO, S. Myocardial infarction and cigarette smoking in women younger than 50 years of age. *Journal of the American Medical Association* 253(20): 2965-2969. May 24-31, 1985.
389. ROSENBERG, L., PALMER, J.R., LESKO, S.M., and SHAPIRO, S. Oral contraceptive use and the risk of myocardial infarction. *American Journal of Epidemiology* 131(6): 1009-1016. Jun. 1990.
390. ROSENBERG, L., PALMER, J.R., ZAUBER, A.G., WARSHAUER, M.E., LEWIS, J.R., STROM, B.L., HARLAP, S., and SHAPIRO, S. A case-control study of oral contraceptive use and invasive epithelial ovarian cancer. *American Journal of Epidemiology* 139(7): 654-661. Apr. 1, 1994.
391. ROSENBERG, L., SHAPIRO, S., SLONE, D., KAUFMAN, D.W., HELMRICH, S.P., MIETTINEN, O.S., STOLLEY, P.D., ROSENBERG, N.B., SHOTTELFELD, D., and ENGLE, J.R. Epithelial ovarian cancer and combination oral contraceptives. *Journal of the American Medical Association* 247(23): 3210-3212. Jun. 18, 1982.
392. ROSENBERG, M.J. Influence of contraceptives on vaginal ecology and infections. In: Horowitz, B.J. and Mardh, P.-A., eds. *Vaginitis and Vaginosis*. New York, Wiley-Liss, Inc. 1991. p. 55-62.
393. ROSENBLAT, K.A., and THOMAS, D.B. Hormonal content of combined oral contraceptives in relation to the reduced risk of endometrial carcinoma. *International Journal of Cancer* 49(6): 870-874. Dec. 2, 1991.
394. ROSENTHAL, G.E., and LANDEFELD, C.S. The relation of chlamydial infection of the cervix to time elapsed from the onset of menses. *Journal of Clinical Epidemiology* 43(1): 15-20. 1990.
395. ROSS, J.D. Is oral contraceptive associated with genital warts? *Genitourinary Medicine* 72(5): 330-333. Oct. 1996.
396. ROYAL COLLEGE OF GENERAL PRACTITIONERS. Oral contraception and thrombo-embolic disease. *Journal of the Royal*



- College of General Practitioners 13: 267-279, 1967.
397. ROYAL COLLEGE OF GENERAL PRACTITIONERS. Oral contraceptives and health. An interim report from the Oral Contraceptive Study of the Royal College of General Practitioners. New York, Pitman, 1974. 100 p.
398. ROYAL COLLEGE OF GENERAL PRACTITIONERS. Effect on hypertension and benign breast disease of progestogen component in combined oral contraceptives. *Lancet* 1(8012): 624. Mar. 19, 1977.
399. ROYAL COLLEGE OF GENERAL PRACTITIONERS. Oral contraceptives, venous thrombosis, and varicose veins. *Journal of the Royal College of General Practitioners* 28(192): 393-399, Jul. 1978.
400. RUDEL, H.W., MAQUEO, M., CALDERONE, J., and MANA-TOU, J.M. Safety and effectiveness of a new low-dose oral contraceptive: A three-year study of 1,000 women. *Journal of Reproductive Medicine* 21(2): 79-88, Aug. 1978.
401. SADEK, S.S., EL SAHAWI, S., and SADEK, W. Effect of the Cu T380 IUD on hemoglobin and iron stores in Egyptian women. *International Journal of Gynecology and Obstetrics* 64(1): 69-70, Jan. 1999.
402. SANKARANARAYANAN, R., WESLEY, R., SOMANATHAN, T., DHAKAL, N., SHYAMALAKUMARY, B., SREEDHAR, N., MAXWELL PARKIN, D., and NAIR, M.K. Visual inspection of the uterine cervix after the application of acetic acid in the detection of cervical carcinoma and its precursors. *Cancer* 83(10): 2150-2156, Nov. 15, 1998.
403. SARACCO, A., MUSICCO, M., NICOLOSI, A., ANGARAN, G., ARICI, C., GAVAZZENI, G., COSTIGLIOLA, P., GAFÀ, S., GERVAISONI, C., LUZZATI, R., PICCININO, F., PUPPO, F., SALASSA, B., SINICCO, A., STELLINI, R., TIRELLI, U., G., T., BIGEVANI, G.M., VISCO, G., ZERBONI, R., and LAZZARIN, L. Man-to-woman sexual transmission of HIV: Longitudinal study of 343 steady partners of infected men. *Journal of Acquired Immune Deficiency Syndromes* 6(5): 497-502, May 1993.
404. SARTORETTO, J.N., ORTEGA-RECIO, J.C., MORAES, R., and NAVAS FILHO, F. Clinical studies with a low dose estrogen-progestogen combination. *Contraception* 15(5): 563-570, May 1977.
405. SAUERBREI, W., BLETNER, M., SCHMOOR, C., BOJAR, H., and SCHUMACHER, M. The effect of oral contraceptive use on the prognosis of node positive breast cancer patients. *European Journal of Cancer* 34(9): 1348-1351, Aug. 1998.
406. SAWYER, R.G., FONG, D., STANKUS, L.R., and MCKELLER, L.A. Emergency contraceptive pills: A survey of use and experiences at college health centers in the Mid-Atlantic United States. *Journal of American College Health* 44(4): 139-144, Jan. 1996.
407. SCHELLEN, A.M. Preliminary experience with a sub-50 combined oral contraceptive, containing 35 micrograms ethinyl oestradiol and 1 mg norethisterone (Neo Con). *Pharmatherapeutica* 2(6): 412-415, 1980.
408. SCHLESSELMAN, J.J. Oral contraceptives in relation to cancer of the breast and reproductive tract: An epidemiological review. *British Journal of Family Planning* 15 (1 Suppl.): 23-33, Apr. 1989.
409. SCHLESSELMAN, J.J. Oral contraceptives and neoplasia of the uterine corpus. *Contraception* 43(6): 557-579, Jun. 1991.
410. SCHLESSELMAN, J.J. Net effect of oral contraceptive use on the risk of cancer in women in the United States. *Obstetrics and Gynecology* 85(5 Pt 1): 793-801, May 1995.
411. SCHWARTZ, S.M., PETITTI, D.B., SISCOVICK, D.S., LONGSTRETH, W.T., SIDNEY, S., RACHUNATHAN, T.E., QUESENBERRY, C.P., and KELAGHAN, J. Stroke and use of low-dose oral contraceptives in young women: A pooled analysis of two US studies. *Stroke* 29(11): 2277-2284, Nov. 1998.
412. SCHWARTZ, S.M., SISCOVICK, D.S., LONGSTRETH, W.T., JR., PSATY, B.M., BEVERLY, R.K., RACHUNATHAN, T.E., LEE, D., and KOEPEL, T.D. Use of low-dose oral contraceptives and stroke in young women. *Annals of Internal Medicine* 127(8 Pt 1): 596-603, Oct. 15, 1997.
413. SCHWINGL, P.J., ORY, H.W., VISNESS, C.M. Estimates of the risk of cardiovascular death attributable to low-dose oral contraceptives in the United States. *American Journal of Obstetrics and Gynecology* 180(1): 241-249, Jan. 1999.
414. SEWANKAMBO, N., GRAY, R.H., WAMER, M.J., FAXTON, L., MCNAIN, D., WABWIE-MANGENI, E., SERWADDI, D., ILLI, C., KIWANUKA, N., HILLIER, S.L., RABIE, L., GAYDOS, C.A., QUINN, T.C., and KONDE-LULE, J. HIV-1 infection associated with abnormal vaginal flora morphology and bacterial vaginosis. *Lancet* 350(9077): 546-550, Aug. 23, 1997.
415. SHAPIRO, S., ROSENBERG, L., SLOAN, D., and KAUFMAN, D.W. Oral-contraceptive use in relation to myocardial infarction. *Lancet* 1(8119): 743-747, Apr. 7, 1979.
416. SHARGL, A.A. Hormone replacement therapy in perimenopausal women with a triphasic contraceptive compound: A three-year prospective study. *International Journal of Fertility* 30(1): 15-28, 1985.
417. SHEN, Q., LIN, D., JIANG, X., LI, H., and ZHANG, Z. Blood pressure changes and hormonal contraceptives. *Contraception* 50(2): 131-141, Aug. 1994.
418. SHENFIELD, G.M. Drug interactions with oral contraceptive preparations. *Medical Journal of Australia* 144(4): 205-211, Feb. 17, 1986.
419. SHENFIELD, G.M. The clinical pharmacology of the oral contraceptive and drugs which alter its activity. *Healthright* 6(2): 27-30, Feb. 1987.
420. SHENFIELD, G.M. The effects of oral contraceptives on therapeutic drugs. *Healthright* 6(3): 28-31, May 1987.
421. SHENFIELD, G.M. Oral contraceptives: Are drug interactions of clinical significance? *Drug Safety* 9(1): 21-37, 1993.
422. SHENFIELD, G.M., and GRIFFIN, J.M. Clinical pharmacokinetics of contraceptive steroids: An update. *Clinical Pharmacokinetics* 20(10): 115-37, Jan. 1991.
423. SHERRIS, J.D. Cervical cancer prevention: A strategic opportunity to improve women's reproductive health. *International Family Planning Perspectives* 25 (Suppl.): S56-S57, Jan. 1999. (Available: <http://www.agi-usa.org/pubs/journals/25S5699.html>). Accessed Mar. 7, 2000.
424. SHOUBNIKOVA, M., HELLBERG, D., NILSSON, S., and MÄRDH, P.-A. Contraceptive use in women with bacterial vaginosis. *Contraception* 55(6): 355-358, Jun. 1997.
425. SIDNEY, S., PETITTI, D.B., QUESENBERRY, C.P., JR., KLATSKY, A.L., ZIEL, H.K., and WOLF, S. Myocardial infarction in users of low-dose oral contraceptives. *Obstetrics and Gynecology* 88(6): 939-944, Dec. 1996.
426. SIKSTRÖM, B., HELLBERG, D., NILSSON, S., BRIHMER, C., and MÄRDH, P.-A. Contraceptive use and reproductive history in women with cervical human papillomavirus infection. *Advances in Contraception* 11(4): 273-284, Dec. 1995.
427. SILBERGELD, S., BRAS, N., and NOBLE, E.P. The menstrual cycle: A double-blind study of symptoms, mood and behavior, and biochemical variables using Enovid and placebo. *Psychosomatic Medicine* 33(5): 411-428, Sep/Oct. 1971.
428. SINEI, S.K., FORTNEY, J.A., KIGONDU, C.S., FELDBLUM, P.J., KUYOH, M., ALLEN, M.Y., and GLOVER, L.H. Contraceptive use and HIV infection in Kenyan family planning clinic attendees. *International Journal of STD and AIDS* 7(1): 65-70, Jan./Feb. 1996.
429. SIRAPAPASIRI, T., THANPRASERTSUK, S., RODKAY, A., SRIVANICHAKORN, S., SAWANPANYALERT, P., and TEMTANARAK, J. Risk factors for HIV among prostitutes in Chiang-mai, Thailand. *AIDS* 5(5): 579-582, May 1991.
430. SKEGG, D.C. Oral contraceptives and neoplasia: An introduction. *Contraception* 43(6): 521-525, Jun. 1991.
431. SLONE, D., SHAPIRO, S., KAUFMAN, D.W., ROSENBERG, L., MIETTINEN, O.S., and STOLLEY, P.D. Risk of myocardial infarction in relation to current and discontinued use of oral contraceptives. *New England Journal of Medicine* 305(8): 420-424, Aug. 20, 1981.
432. SNOWBALL, S., and TAYLOR, W. Effects of short-term treatment with a combined oestrogen-progestin oral contraceptive on biliary lipids and cholesterol saturation index in young women. *Journal of Steroid Biochemistry* 22(2): 257-261, Feb. 1985.
433. SOLVELL, L., and NILSSON, L. A clinical study on a sequential oral contraceptive-Ovisec. *Acta Obstetrica et Gynecologica Scandinavica* 47(Suppl. 6): 3-25, 1968.
434. SPEIDEL, J.J., RAVENHOLT, R.T., and IRVINE, M.E. Liberalized policies for distribution of oral contraceptives. *Studies in Family Planning* 5(2): 62-67, Feb. 1974.
435. SPELLACY, W.N., and BIRK, S.A. The effect of intrauterine devices, oral contraceptives, estrogens, and progestogens on blood pressure. *American Journal of Obstetrics and Gynecology* 112(7): 912-919, Apr. 1972.
436. SPELLACY, W.N., KALRA, P.S., BUHI, W.C., and BIRK, S.A. Pituitary and ovarian responsiveness to a graded gonadotropin releasing factor stimulation test in women using a low-estrogen or a regular type of oral contraceptive. *American Journal of Obstetrics and Gynecology* 137(1): 109-115, May 1, 1980.
437. SPEROFF, L., ARCHER, D.F., and MISHELL, Jr., D.R. Multiphasic and monophasic OCs: Is there a difference? *Contemporary Obstetrics and Gynecology* 32(Special Issue): 124-134, 137-145, Sep. 15, 1988.
438. SPEROFF, L., CLASS, R., and KASE, N. *Clinical Gynecologic Endocrinology and Infertility*. 4th ed. Baltimore, Williams and Wilkins, 1994.
439. SPINILLO, A., CORINI, G., PIAZZI, G., BALTARO, F., MONACO, A., and ZARA, F. The impact of oral contraception on chlamydial infection among patients with pelvic inflammatory disease. *Contraception* 54(3): 163-168, Sep. 1996.
440. SPITZER, W.O., LEWIS, M.A., HEINEMANN, L.A., THOROGOOD, M., and MACRAE, K.D. Third generation oral contraceptives and risk of venous thromboembolic disorders: An international case-control study. *British Medical Journal* 312(7023): 83-88, Jan. 13, 1996.
441. STADEL, B.V. Oral contraceptives and cardiovascular disease. (Second of two parts). *New England Journal of Medicine* 305(12): 672-677, Sep. 17, 1981.
442. STAMPER, M.J., WILLET, W.C., COLDITZ, G.A., SPEIZER, F.E., and HENNEKENS, C.H. A prospective study of past use of oral contraceptive agents and risk of cardiovascular diseases. *New England Journal of Medicine* 319(20): 1313-1317, Nov. 17, 1988.
443. STAMPER, M.J., WILLET, W.C., COLDITZ, G.A., SPEIZER, F.E., and HENNEKENS, C.H. Past use of oral contraceptives and cardiovascular disease: A meta-analysis in the context of the Nurses' Health Study. *American Journal of Obstetrics and Gynecology* 163(1 Pt. 2): 285-291, Jul. 1990.
444. STANFORD, J.L., RAY, R.M., and THOMAS, D.B. Combined oral contraceptives and liver cancer: The WHO Collaborative Study of Neoplasia and Steroid Contraceptives. *International Journal of Cancer* 43(2): 254-259, Feb. 15, 1989.
445. STEPHENSON, J.M. Systematic review of hormonal contraception and risk of HIV transmission: When to resist meta-analysis. *AIDS* 12(6): 545-553, Apr. 16, 1998.
446. STOWALL, T., KELLERMAN, A., LING, F., and BUSTER, B. Emergency department diagnosis of ectopic pregnancy. *Annals of Emergency Medicine* 19(10): 1098-1103, Oct. 19, 1990.
447. SUSSA, S., BLAIS, L., SPITZER, W.O., CUSSON, J., LEWIS, M., and HEINEMANN, L. First-time use of newer oral contraceptives and the risk of venous thromboembolism. *Contraception* 56(3): 141-146, Sep. 1997.
448. SWAFER, M.L., WESTLUND, P., JOHANSSON, E., and BYGDEMANN, M. Effect of post-coital contraceptive methods on the endometrium and the menstrual cycle. *Journal of Human Nutrition* 75(8): 738-744, Sep. 1996.
449. SYRJÄNEN, K., VÄYRYNEN, M., CASTREN, O., YLISKOSKI, M., MÄNTYJÄRVI, R., PYRÖNEN, S., and SAARIKOSKI, S. Sexual behaviour of women with human papillomavirus (HPV) lesions of the uterine cervix. *British Journal of Venereal Disease* 60(4): 243-248, Aug. 1984.
450. SZOKA, P.R., and EDGREN, R.A. Drug interactions with oral contraceptives: Compilation and analysis of an adverse experience report database. *Fertility and Sterility* 49(5 Suppl. 2): 318-385, May 1988.
451. TAHA, T.E., HOOVER, D.R., DALLABETTA, G.A., KUMWENDA, N.I., MTIMAVALE, L.A.R., YANG, L.-P., LIOMBA, G.N., BROADHEAD, R.L., CHIPHANGWI, J.D., and MIOTTI, P.G. Bacterial vaginosis and disturbances of vaginal flora: Association with increased acquisition of HIV. *AIDS* 12(13): 1699-1706, 1998.
452. TANKEYOON, M., DUSITSIN, N., CHALAPATI, S., KOETSAWANG, S., KIRIAT, O., MUKULKARN, P., PANPRAT, C., GELLEN, J.J., GAMSU, H.R., and FINUCANE, E. Effects of hormonal contraceptives on breast milk composition and infant growth. *Studies in Family Planning* 19(6 Pt. 1): 361-369, Nov/Dec. 1988.
453. TASK FORCE ON POSTOVULATORY METHODS OF FERTILITY REGULATION. Randomised controlled trial of levonorgestrel versus the Yuzpe regimen of combined oral contraceptives for emergency contraception. *Lancet* 352(9126): 428-433, Aug. 8, 1998.
454. TATE, P. Minimising risk in contraception. *Practitioner* 241(1579): 571-572, 574, 576, 580, Oct. 1997.
455. TAVANI, A., NEGRI, E., PARAZZINI, F., FRANCESCHI, S., and LA VECCHIA, C. Female hormone utilisation and risk of hepatocellular carcinoma. *British Journal of Cancer* 67(3): 635-637, Mar. 1993.
456. TECHNICAL GUIDANCE/COMPETENCE WORKING GROUP. Recommendations for updating selected practices in contraceptive use. Volume II. Gaines, M., ed. US Agency for International Development, World Health Organization, Sep. 1997. 260 p. (Available: <http://www.reproline.jhu.edu/english/6read/6multi/6tmgw/6tmgw.htm>). Accessed Mar. 7, 2000.
457. THIERY, M., VAN KETS, H., DEMOL, R., and MOLITOR, M.P. Clinical trial of a new oral contraceptive with a low oestrogen dosage: Restovar. *Journal of International Medical Research* 3(6): 279-283, 1975.
458. THUIS, C., and KNIPSCHILD, P. Oral contraceptives and the risk of gallbladder disease: A meta-analysis. *American Journal of Public Health* 83(8): 1113-1120, Aug. 1993.
459. THIRY, L., VOKAER, R., DETREMERIE, O., BOLLEN, A., and HALLEZ, S. Contraception, papillomavirus, and cervical cancer. *Lancet* 339(8793): 616, Mar. 7, 1992.
460. THOMAS, D.B. The WHO Collaborative Study of Neoplasia and Steroid Contraceptives: The influence of combined oral contraceptives on risk of neoplasms in developing and developed countries. *Contraception* 43(6): 695-710, Jun. 1991.
461. THOMAS, D.B., and RAY, R.M. Depot-medroxyprogesterone acetate (DMPA) and risk of endometrial cancer. The WHO Collaborative Study of Neoplasia and Steroid Contraceptives. *International Journal of Cancer* 49: 186-190, 1991.
462. THOMAS, D.B., and RAY, R.M. Oral contraceptives and invasive adenocarcinomas and adenocarcinomas of the uterine cervix. *American Journal of Epidemiology* 144(3): 281-289, Aug. 1, 1996.
463. THOROGOOD, M. Oral contraceptives and myocardial infarction: New evidence leaves unanswered questions. *Thrombosis and Haemostasis* 78(1): 334-338, Jul. 1997.
464. THOROGOOD, M. Stroke and steroid hormonal contraception. *Contraception* 57(3): 157-167, Mar. 1998.
465. THOROGOOD, M., MANN, J., and MURPHY, M. Is oral contraceptive use still associated with an increased risk of myocardial infarction? Report of a case-control study. *British Journal of Obstetrics and Gynecology* 98(8): 1245-1253.
466. THOROGOOD, M., and VILLARD-MACKINTOSH, L. Combined oral contraceptives: Risks and benefits. *British Medical Bulletin* 49(1): 124-139, Jan. 1993.
467. TIKKANEN, M.J., and NIKKILA, E.A. Oral contraceptives and lipoprotein metabolism. *Journal of Reproductive Medicine* 31(9 Suppl.): 898-905, Sep. 1986.
468. TROISI, R., SCHAIER, C., CHOW, W.H., SCHATZKIN, A., BRINTON, L.A., and FRAUMENI, Jr., J.F. Reproductive factors, oral contraceptive use, and risk of colorectal cancer. *Epidemiology* 8(1): 75-79, Jan. 1997.
469. TRUSSELL, J. Efficacy of ECPs. Personal communication, Nov. 30, 1999.
470. TRUSSELL, J., DURAN, V., SHOCHET, T., and MOORE, K. Access to emergency contraception. *Obstetrics and Gynecology* 95(2): 267-270, Feb. 2000.
471. TRUSSELL, J., and RAYMOND, E.G. Statistical evidence about the mechanism of action of the Yuzpe regimen of emergency contraception. *Obstetrics and Gynecology* 93(5): 872-876, May 1999.
472. TRUSSELL, J., RODRIGUEZ, G., and ELLERTSON, C. Updated estimates of the effectiveness of the Yuzpe regimen of emergency contraception. *Contraception* 59(3): 147-151, Mar. 1999.
473. TRUSSELL, J., STEWART, F., GUEST, R., and HATCHER, R.A. Emergency contraceptive pills: A simple proposal to reduce unintended pregnancies. *Family Planning Perspectives* 24(6): 269-273, Nov/Dec. 1992.
474. TZOUNOU, A., DAY, N.E., TRICHOPOULOS, D., WALKER, A., SALIARAKI, M., PAPAPOSTOLOU, M., and POLYCHRONOPOULOU, A. The epidemiology of ovarian cancer in Greece: A case-control study. *European Journal of Cancer and Clinical Oncology* 20(8): 1045-1052, Aug. 1984.
475. TZOURIO, C., TEHINDRANARIVLO, A., IGLESIAS, S., ALPEROVITCH, A., CHEDRU, F., D'ANGLEJAN-CHATILLON, J., and BOUSSER, M.G. Case-control study of migraine and risk of ischaemic stroke in young women. *British Medical Journal* 310(6983): 830-833, Apr. 1, 1995.
476. UNITED NATIONS POPULATION FUND (UNFPA). Emergency reproductive health kits en route to Kosovo refugees: UNFPA (Website). <http://www.unfpa.org/news/pressroom/1999/kosovo.htm>. Accessed Mar. 7, 2000.
477. UNITED NATIONS HIGH COMMISSIONER FOR REFUGEES (UNHCR), UNITED NATIONS FUND FOR POPULATION ACTIVI-



- TIES, and WORLD HEALTH ORGANIZATION. Sexual and gender-based violence. In: Reproductive Health in Refugee Situations: An Inter-Agency Field Manual. UNHCR, 1999. p. 35-46.
478. UNITED STATES CENTERS FOR DISEASE CONTROL. Current trends in ectopic pregnancy United States, 1990-1992. Morbidity and Mortality Weekly Report 44(3): 46-48. Jan. 27, 1995.
479. UNIVERSITY OF ZIMBABWE/JHPIEGO CERVICAL CANCER PROJECT. Visual inspection with acetic acid for cervical cancer screening: Test qualities in a primary-care setting. Lancet 353(9156): 869-873. Mar. 13, 1999.
480. URSIN, G., ROSS, R.K., SULLIVAN-HALLEY, J., HANISCH, R., HENDERSON, B., and BERNSTEIN, L. Use of oral contraceptives and risk of breast cancer in young women. Breast Cancer Research and Treatment 50(2): 175-184. Jul. 1998.
481. US FOOD AND DRUG ADMINISTRATION. Certain combined oral contraceptives for use as postcoital emergency contraception; Notice. Federal Register 62(37). Department of Health and Human Services. Feb. 25, 1997.
482. UTIAN, W.H. Oral contraceptive formulations—Influence on user compliance and reliability of the method. Singapore Journal of Obstetrics and Gynaecology 15(1 Suppl.): 6-13. Mar. 1984.
483. VALLS, C., ANDIA, E., SANCHEZ, A., GUMA, A., and SER-RANO, T. Hyperenhancing focal liver lesions: Differential diagnosis with helical CT. American Journal of Roentgenology 173(3): 606-611. Sep. 1999.
484. VANDENBROEK, N. Anaemia in pregnancy in developing countries. British Journal of Obstetrics and Gynaecology 105(4): 385-390. Apr. 1998.
485. VAN LOOK, P.F. Lactational amenorrhoea method for family planning. Provides high protection from pregnancy for the first six months after delivery. British Medical Journal 313(7062): 893-894. Oct. 12, 1996.
486. VAN LOOK, P.F.A. and STEWART, F. Emergency contraception. In: HATCHER, R.A., TRUSSELL, J., STEWART, F., CATES Jr., W., STEWART, G.K., GUEST, F., and KOWAL, D. Contraceptive Technology. 17th ed. New York, Ardent Media, Inc. 1998. p. 277-295.
487. VANDENVELDE, C. and VAN BEERS, D. Risk factors inducing the persistence of high-risk genital papillomaviruses in the normal cervix. Journal of Medical Virology 38(3): 226-232. Nov. 1992.
488. VASILAKIS, C., JICK, S.S., and JICK, H. The risk of venous thromboembolism in users of postcoital contraceptive pills. Contraception 59(2): 79-83. Feb. 1999.
489. VERESS, G., CSIKY-MESZAROS, T., CZEGLÉDY, J., and GERGELY, L. Oral contraceptive use and human papillomavirus infection in women without abnormal cytological results. Medical Microbiology and Immunology 181(4): 181-189. 1992.
490. VESSEY, M., DOLL, R., PETO, R., JOHNSON, B., and WIGGINS, P. A long-term follow-up study of women using different methods of contraception—An interim report. Journal of Biosocial Science 8(4): 375-427. Oct. 1976.
491. VESSEY, M. and GRICE, D. Carcinoma of the cervix and oral contraceptives: Epidemiological studies. Biomedicine and Pharmacotherapy 43(3): 157-160. 1989.
492. VESSEY, M., MANT, J., and PAINTER, R. Oral contraception and other factors in relation to hospital referral for fracture: Findings in a large cohort study. Contraception 57(4): 231-235. Apr. 1998.
493. VESSEY, M., METCALFE, A., WELLS, C., MCPHERSON, K., WESTHOFF, C., and YEATES, D. Ovarian neoplasms, functional ovarian cysts, and oral contraceptives. British Medical Journal 294(6586): 1518-1520. Jun. 13, 1987.
494. VESSEY, M. and PAINTER, R. Oral contraceptive use and benign gallbladder disease, revisited. Contraception 50(2): 167-173. Aug. 1994.
495. VESSEY, M., PAINTER, R., and MANT, J. Oral contraception and other factors in relation to hospital referral for menstrual problems without known underlying cause: Findings in a large cohort study. British Journal of Family Planning 22(4): 166-169. Jan. 1997.
496. VESSEY, M.P. and DOLL, R. Investigation of relation between use of oral contraceptive and thromboembolic disease. British Medical Journal 2(5599): 199-205. Apr. 27, 1968.
497. VESSEY, M.P., LAWLESS, M., and YEATES, D. Oral contraceptives and stroke: Findings in a large prospective study. British Medical Journal 289(6444): 530-531. Sep. 1, 1984.
498. VESSEY, M.P., LAWLESS, M., YEATES, D., and MCPHERSON, K. Progestogen-only oral contraception: Findings in a large prospective study with special reference to effectiveness. British Journal of Family Planning 10(4): 117-121. Jan. 1985.
499. VIRTAVUO, T., PUNNONEN, R., KALLIO, H., MANNER, P., REHN, K., KANNEL, L., APAJALAHTE, E., and HUSA, L. A multicentre trial with a low-dose combination type oral contraceptive. Pharmatherapeutica 118(1): 535-539. 1977.
500. VISNESS, C.M. and RIVERA, R. Progestin-only pill use and pill switching during breastfeeding. Contraception 51(5): 279-281. May 1995.
501. VMEIJEN, I.E. and GRIMES, D.A. Oral contraceptives and primary liver cancer: temporal trends in three countries. Obstetrics and Gynecology 88(6): 945-949. Dec. 1996.
502. WALBOOMERS, J.M.M., JACOBS, M.V., NIANJOS, M.M., BOSCH, F.X., KUMMER, J.A., SHAH, K.V., SNIJDERS, P.J.F., PETO, J., MEIJER, C.J.L.M., and MUÑOZ, N. Human papillomavirus is a necessary cause of invasive cervical cancer worldwide. Journal of Pathology 189(1): 112-119. Sep. 1999.
503. WALKER, A.M. Newer oral contraceptives and the risk of venous thromboembolism. Contraception 57(3): 169-181. Mar. 1998.
504. WANG, C.C., KREISS, J.K., and REILLY, M. Risk of HIV infection in oral contraceptive pill users: A meta-analysis. Journal of Acquired Immune Deficiency Syndromes 21(1): 51-58. May 1, 1999.
505. WASHINGTON, A.E., ARAL, S.O., WILNER-HANSEN, P., GRIMES, D.A., and HOLMES, K.K. Assessing risk for pelvic inflammatory disease and its sequelae. Journal of the American Medical Association 266(18): 2581-2586. Nov. 13, 1991.
506. WASHINGTON, A.E., GOVE, S., SCHACHTER, J., and SWEET, R.L. Oral contraceptives, *Chlamydia trachomatis* infection, and pelvic inflammatory disease. A word of caution about protection. Journal of the American Medical Association 253(15): 2246-2250. Apr. 19, 1985.
507. WAWER, M.J., SEWANKAMBO, N.K., SERWADDA, D., QUINN, T.C., PAXTON, L.A., KIWANUKA, N., WABWIRE-MANGEN, F., LI, C., LUTALO, T., NALUGODA, F., GAYDOS, C.A., MOULTON, L.H., MEEHAN, M.O., AHMED, S., RAKAI PROJECT STUDY GROUP, and GRAY, R.H. Control of sexually transmitted diseases for AIDS prevention in Uganda: A randomised community trial. Lancet 353(9152): 525-535. Feb. 13, 1999.
508. WEAVER, K. and GLASIER, G. Interaction between broad-spectrum antibiotics and the combined oral contraceptive pill: A literature review. Contraception 59(2): 71-78. Feb. 1999.
509. WEINSTOCK, H., BOLAN, G.A., KOHN, R., BALLADARES, C., BACK, A., and OLIVA, G. *Chlamydia trachomatis* infection in women: A need for universal screening in high prevalence populations. American Journal of Epidemiology 135(1): 41-47. Jan. 1, 1992.
510. WEIR, R.J., BRIGGS, E., MACK, A., NAISMITH, L., TAYLOR, L., and WILSON, E. Blood pressure in women taking oral contraceptives. British Medical Journal 1(5907): 533-535. Mar. 23, 1974.
511. WEIR, R.J., DAVIES, D.L., FRASER, R., MORTON, J.I., TREE, M., and WILSON, A. Contraceptive steroids and hypertension. Journal of Steroid Biochemistry 6(6): 961-964. Jun. 1975.
512. WEISBERG, E. Triphasic: Have they fulfilled their promise? [editorial]. Current Therapeutics 33(1): 11-16. Jan. 1992.
513. WEISBERG, E., FRASER, I.S., CARRICK, S.E., and WILDE, F.M. Emergency contraception: General practitioner knowledge, attitudes and practices in New South Wales. Medical Journal of Australia 162(2): 136-138. Feb. 6, 1995.
514. WEISS, N.S., DALING, J.R., and CHOW, W.H. Incidence of cancer of the large bowel in women in relation to reproductive and hormonal factors. Journal of the National Cancer Institute 67(1): 57-60. Jul. 1981.
515. WEISS, N.S., LYON, J.L., LIFF, J.M., VOLLMER, W.M., and DALING, J.R. Incidence of ovarian cancer in relation to the use of oral contraceptives. International Journal of Cancer 28(6): 669-671. Dec. 15, 1981.
516. WEISS, N.S. and SAYVETZ, T.A. Incidence of endometrial cancer in relation to the use of oral contraceptives. New England Journal of Medicine 302(10): 551-554. Mar. 6, 1980.
517. WELLS, E. (Consortium for Emergency Contraception) [Provision of ECPs beyond 72 hours] Personal communication, Feb. 3, 2000.
518. WELLS, E., CROOK, B., and MULLER, N. Emergency contraception: A resource manual for providers. Seattle, Washington, Program for Appropriate Technology in Health, May 1997. 34 p.
519. WEST, C. Changes in fertility. Demos 10: 16-18. 1997.
520. WEST, C.P. The acceptability of a progestogen-only contraceptive during breast-feeding. Contraception 27(6): 563-569. Jun. 1983.
521. WESTHOFF, C.T. Oral contraceptives and breast cancer—Resolution emerges [Editorial]. Contraception 54(3 Suppl.): i-ii. Sep. 1996.
522. WHARTON, C. and BLACKBURN, R. Lower dose pills. Population Reports, Series A, No. 7. Baltimore, Johns Hopkins School of Public Health, Population Information Program, Nov. 1988. 31 p.
523. WHO (WORLD HEALTH ORGANIZATION). Smoking and women: The next wave of the tobacco epidemic. Fact Sheet N 176. (Website). <http://www.who.int/inf-fs/en/fact176.html>. Aug. 1997. Accessed Mar. 7, 2000.
524. WILLEIT, W.C., BAIN, C., HENNEKENS, C.H., ROSNER, B., and SPIELER, I.F. Oral contraceptives and risk of ovarian cancer. Cancer 48(8): 1684-1687. Oct. 15, 1981.
525. WILSON, E.S., CRUICKSHANK, J., MCMASTER, M., and WEIR, R.J. A prospective controlled study of the effect on blood pressure of contraceptive preparations containing different types and dosages of progestogen. British Journal of Obstetrics and Gynaecology 91(12): 1254-1260. Dec. 1984.
526. WINGRAVE, S.J. and KAY, C.R. Oral contraceptives and gallbladder disease. Royal College of General Practitioners' Oral Contraception Study. Lancet 2(8305): 957-959. Oct. 30, 1982.
527. WINKELSTEIN JR., W. Smoking and cervical cancer: Current status: A review. American Journal of Epidemiology 131(6): 945-957. Jun. 1990.
528. WOOD, R., BOTTING, B., and DUNNELL, K. Trends in conceptions before and after the 1995 pill scare. Office for National Statistics, United Kingdom, Autumn, 1997.
529. WORLD HEALTH ORGANIZATION (WHO). Progestogen-only contraceptives during lactation: II. Infant development. Contraception 50(1): 55-68. Jul. 1994.
530. WORLD HEALTH ORGANIZATION (WHO). The prevalence of nutritional anaemia in women in developing countries: A literature review. Geneva, WHO, 1979. 118 p.
531. WORLD HEALTH ORGANIZATION (WHO). A randomized, double-blind study of six combined oral contraceptives. Contraception 25(3): 231-241. Mar. 1982.
532. WORLD HEALTH ORGANIZATION (WHO). The WHO multicentre trial of the vasopressor effects of combined oral contraceptives: I. Comparisons with IUD. Contraception 40(2): 129-145. Aug. 1989.
533. WORLD HEALTH ORGANIZATION (WHO). Oral contraceptives and neoplasia: Report of a WHO scientific group. Geneva, WHO, 1992. (WHO Technical Report Series No. 817) 52 p.
534. WORLD HEALTH ORGANIZATION (WHO). The prevalence of anaemia in women: A tabulation of available information. Geneva, WHO, 1992. (2nd ed.) 100 p.
535. WORLD HEALTH ORGANIZATION (WHO). Haemorrhagic stroke, overall stroke risk, and combined oral contraceptives: Results of an international, multicentre, case-control study. Lancet 348(9026): 505-510. Aug. 24, 1996.
536. WORLD HEALTH ORGANIZATION (WHO). Improving access to quality care in family planning: Medical eligibility criteria for contraceptive use. Geneva, WHO, 1996. 143 p.
537. WORLD HEALTH ORGANIZATION (WHO). Acute myocardial infarction and combined oral contraceptives: Results of an international multicentre case-control study. Lancet 349(9060): 1202-1209. Apr. 26, 1997.
538. WORLD HEALTH ORGANIZATION (WHO). Cardiovascular disease and steroid hormone contraception: Report of a WHO scientific group. Geneva, WHO, 1997. (WHO Technical Report Series No. 877) 90 p.
539. WORLD HEALTH ORGANIZATION (WHO). Emergency contraception: A guide for service delivery. Geneva, WHO, 1998. 60 p.
540. WORLD HEALTH ORGANIZATION (WHO). World health report 1999: Making a difference. Geneva, WHO, 1999. 121 p.
541. WOUTERSZ, T.B. Three and one-half years' experience with a lower-dose combination oral contraceptive. Journal of Reproductive Medicine 16(6): 338-344. Jun. 1976.
542. WYNN, V. Effect of progesterone and progestins on carbohydrate metabolism. In: Bardin, C., Milgrom, E., and Mauvais-Jarvis, P., eds. Progesterone and progestins. New York, Raven Press. p. 395-410.
543. WYNN, V. and GODSAND, I. Effects of oral contraceptives on carbohydrate metabolism. Journal of Reproductive Medicine 31(9 Suppl.): 892-897. Sep. 1986.
544. YE, Z., THOMAS, D.B., RAY, R.M., and THE WHO COLLABORATIVE STUDY OF NEOPLASIA AND STEROID CONTRACEPTIVES. Combined oral contraceptives and risk of cervical carcinoma in situ. International Journal of Epidemiology 24(1): 19-26. Feb. 1995.
545. YLITALO, N., SORESENSEN, P., JOSEFSSON, A., FRISCH, M., SPAREN, P., PONTEN, J., GYLLENSTEN, U., MELBYE, M., and ADAMI, H.O. Smoking and oral contraceptives as risk factors for cervical carcinoma in situ. International Journal of Cancer 81(3): 357-365. May 5, 1999.
546. YU, M.C., TONG, M.J., GOVINDARAJAN, S., and HENDERSON, B.E. Nonviral risk factors for hepatocellular carcinoma in a low-risk population, the non-Asians of Los Angeles County, California. Journal of the National Cancer Institute 83(24): 1820-1826. Dec. 18, 1991.
547. YUZZE, A.A., THURLOW, H.J., and LANCEE, W.J. Postcoital contraception—Follow-on to a pilot study [unpublished]. May 1974. 15 p.
548. YUZZE, A.A., THURLOW, H.J., RAMZY, I., and Leyshon, J.I. Post coital contraception: A pilot study. Journal of Reproductive Medicine 13(2): 53-58. Aug. 1974.
549. ZACHARIAS, S., AGUILERA, E., ASSENZO, J.R., and ZANARTU, J. Effects of hormonal and nonhormonal contraceptives on lactation and incidence of pregnancy. Contraception 33(3): 203-213. Mar. 1986.

## ADDENDA

552. LABBOK, M.H., PEREZ, A., VALDES, V., SEVILLA, F., WADE, K., LAUKARAN, V.H., COONEY, K.A., COLY, S., SANDERS, C., and QUEENAN, J.T. The Lactational Amenorrhea Method (LAM): Apostamut introductory family planning method with policy and program implications. Advances in Contraception 10(2): 93-109. Jun. 1994.
553. MAHMOUD, E.A., HAMAD, E.E., OLSSON, S.E., and MARDH, P.A. Antichlamydial activity of cervical secretion in different phases of the menstrual cycle and influence of hormonal contraceptives. Contraception 49(3): 265-275. Mar. 1994.
554. VANDENBROUCKE, J.P., HELMERHORST, F.M., BLOEMENKAMP, K.W., and ROSENDAAL, F.R. Third-generation oral contraceptive and deep venous thrombosis: from epidemiologic controversy to new insight in coagulation. American Journal of Obstetrics and Gynecology 177(4): 887-891. Oct. 1997.
555. WORLD HEALTH ORGANIZATION (WHO). The World Health Organization multinational study of breast-feeding and lactational amenorrhea. III. Pregnancy during breastfeeding. Fertility and Sterility 72(3): 491-499. Sep. 1999.
556. SCHLESSELMAN, J.J. and FARLEY, T.M.M. Risk of cardiovascular disease in relation to oral contraception use with and without blood pressure screening. Draft, Feb. 2000. Presented to meeting on Improving Access and Quality of Care in Family Planning: Medical Eligibility Criteria for Contraceptive Use, World Health Organization, Geneva, Mar. 8-10, 2000. 27 p.
557. WORLD HEALTH ORGANIZATION (WHO). Improving access and quality of care in family planning: Medical eligibility for contraceptive use. Second ed. [Draft] Geneva, WHO, 2000.

ISSN 0887-0241



# POPULATION REPORTS

**Population Reports** are free in any quantity to developing countries. In USA and other developed countries, multiple copies are US\$2.00 each; full set of reports in print, \$35.00; with binder, \$40.00. Send payment in US\$ with order. **Population Reports** in print in English are listed below. Many are also available in French, Portuguese, and Spanish, as indicated by abbreviations after each title on the order form below.

## POPLINE Digital Services

**Popline Digital Services (PDS)** produces several information products:

**POPLINE** is the world's largest bibliographic database on population, family planning, and related health issues.

**POPLINE** is available on CD-ROM, on the Internet at: <http://www.jhuccp.org/popline>, or

**POPLINE** searches can be requested from **Popline Digital Services**.

**CONDOMS CD-ROM** is a multimedia compilation of information, education, and communication materials on condoms. It is an "idea bank" for reproductive health professionals.

**HIM CD-ROM** (Helping Involve Men) provides the core collection of literature on the participation of men in reproductive health programs. Contact **PDS** at the address below for information on availability of these products.

**TO ORDER POPULATION REPORTS please complete the form below. (PRINT or TYPE clearly.)**

**Mail to:**

**Population Information Program, The Johns Hopkins School of Public Health**

**111 Market Place, Suite 310, Baltimore, MD 21202, USA**

**Fax: (410) 659-2645 E-mail: [PopRepts@jhuccp.org](mailto:PopRepts@jhuccp.org) Internet site: <http://www.jhuccp.org>**



**Family name**

**Given name**

**Organization**

**Address**

### Population Reports in Print

- ☐ Send \_\_\_ copies of each future issue of **Population Reports**.
- ☐ I am already on the **Population Reports** mailing list.
- ☐ Send me a binder (in developed countries, US\$7.00).
- Language: ☐ English ☐ French ☐ Portuguese ☐ Spanish.
- Check (✓) the issues you want:

- \_\_\_ J-41 Meeting the Needs of Young Adults [1995] (F,P,S)
- \_\_\_ J-42 Helping the News Media Cover Family Planning [1995] (F,S)
- \_\_\_ J-43 Meeting Unmet Need: New Strategies [1996] (F,S)
- \_\_\_ J-44 Family Planning Methods: New Guidance [1996] (F,S)
- \_\_\_ J-45 People Who Move: New Reproductive Health Focus [1997] (F,S)
- \_\_\_ J-46 Reproductive Health: New Perspectives on Men's Participation [1998] (F,S)
- \_\_\_ J-47 Family Planning Programs: Improving Quality [1998] (F,P,S)
- \_\_\_ J-48 GATHER Guide to Counseling [1998] (F,S)
- \_\_\_ J-49 Why Family Planning Matters [1999]

#### ORAL CONTRACEPTIVES—Series A

- \_\_\_ A-8 Counseling Clients About the Pill [1990] (F,S)
- \_\_\_ A-9 Oral Contraceptives—An Update [2000]

#### INTRAUTERINE DEVICES—Series B

- \_\_\_ B-6 IUDs—An Update [1995] (F,P,S)

#### STERILIZATION, FEMALE—Series C

- \_\_\_ C-10 Voluntary Female Sterilization: Number One and Growing [1991] (F,S)

#### STERILIZATION, MALE—Series D

- \_\_\_ D-5 Vasectomy: New Opportunities [1992] (F,S)
- \_\_\_ D-5 Guide: Quick Guide to Vasectomy Counseling [1992] (F,S)

#### BARRIER METHODS—Series H

- \_\_\_ H-8 Condoms—Now More Than Ever [1991] (F,S)
- \_\_\_ H-9 Closing the Condom Gap [1999]

#### FAMILY PLANNING PROGRAMS—Series J

- \_\_\_ J-27 Healthier Mothers and Children Through Family Planning [1984]
- \_\_\_ J-38 Poster: Entertainment Educates! [1990]
- \_\_\_ J-39 Paying for Family Planning [1991] (F,S)
- \_\_\_ J-40 Making Programs Work [1994] (F,S)
- \_\_\_ J-40 Poster: Family Planning Helps Everyone [1994] (F,S)

#### INJECTABLES AND IMPLANTS—Series K

- \_\_\_ K-4 Decisions for Norplant Programs [1992] (F,S)
- \_\_\_ K-4 Guide: Guide to Norplant Counseling [1992] (F,S)
- \_\_\_ K-4 Fact sheet: Norplant at a Glance [1992] (F,S)
- \_\_\_ K-5 New Era for Injectables [1995] (F,P,S)
- \_\_\_ K-5 Guide: Guide to Counseling on Injectables [1995] (F,P,S)
- \_\_\_ K-5 Fact sheet: DMPA at a Glance [1995] (F,P,S)

#### ISSUES IN WORLD HEALTH—Series L

- \_\_\_ L-9 Controlling Sexually Transmitted Diseases [1993] (F,S)
- \_\_\_ L-10 Care for Postabortion Complications: Saving Women's Lives [1997] (F,S)
- \_\_\_ L-10 Wall chart: Family Planning After Postabortion Treatment [1997] (F,S)
- \_\_\_ L-11 Ending Violence Against Women [1999]

#### SPECIAL TOPICS—Series M

- \_\_\_ M-10 The Environment & Population Growth: Decade for Action [1992] (F,S)
- \_\_\_ M-11 The Reproductive Revolution: New Survey Findings [1992] (F,S)
- \_\_\_ M-12 Opportunities for Women Through Reproductive Choice [1994] (F,P,S)
- \_\_\_ M-13 Winning the Food Race [1997] (F,S)
- \_\_\_ M-14 Solutions for a Water-Short World [1998] (F,S)

### POPLINE Digital Services

Send more information on these reproductive health information products:

- ☐ POPLINE ☐ POPLINE CD-ROM ☐ CONDOMS CD-ROM
- ☐ HIM CD-ROM ☐ DOCUMENT DELIVERY

